```
=> file registry
FILE 'REGISTRY' ENTERED AT 09:48:41 ON 20 FEB 2008
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   19 FEB 2008  HIGHEST RN 1004621-14-0
DICTIONARY FILE UPDATES:  19 FEB 2008  HIGHEST RN 1004621-14-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> file zcaplus
FILE 'ZCAPLUS' ENTERED AT 09:48:47 ON 20 FEB 2008
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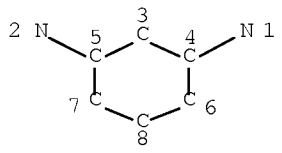
FILE COVERS 1907 - 20 Feb 2008  VOL 148 ISS 8
FILE LAST UPDATED: 19 Feb 2008  (20080219/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCAPLUS' FILE

=> d stat que L29
L6              STR
```



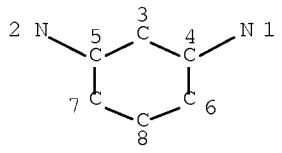
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 8

STEREO ATTRIBUTES: NONE

L8	103	SEA FILE=REGISTRY FAM FUL L6
L10	23	SEA FILE=REGISTRY ABB=ON PLU=ON L8 AND CL/ELS
L11	4	SEA FILE=REGISTRY ABB=ON PLU=ON L10 AND ?HYDROCHLORID?/CNS
L12	5	SEA FILE=ZCAPLUS ABB=ON PLU=ON L11
L14	422537	SEA FILE=ZCAPLUS ABB=ON PLU=ON ?ISOMER?/BI
L15	135031	SEA FILE=ZCAPLUS ABB=ON PLU=ON ?CHIRAL?/BI
L16	288070	SEA FILE=ZCAPLUS ABB=ON PLU=ON ?STEREO?/BI
L17	93962	SEA FILE=ZCAPLUS ABB=ON PLU=ON ?ENANTIO?/BI
L18	382970	SEA FILE=ZCAPLUS ABB=ON PLU=ON ?RESOLUTION?/BI
L19	210367	SEA FILE=ZCAPLUS ABB=ON PLU=ON ASYMMETR?/BI
L20	3	SEA FILE=ZCAPLUS ABB=ON PLU=ON L12 AND L14
L21	0	SEA FILE=ZCAPLUS ABB=ON PLU=ON L12 AND L15
L22	1	SEA FILE=ZCAPLUS ABB=ON PLU=ON L12 AND L16
L23	0	SEA FILE=ZCAPLUS ABB=ON PLU=ON L12 AND L17
L24	1	SEA FILE=ZCAPLUS ABB=ON PLU=ON L12 AND L18
L25	0	SEA FILE=ZCAPLUS ABB=ON PLU=ON L12 AND L19
L26	3	SEA FILE=ZCAPLUS ABB=ON PLU=ON (L20 OR L21 OR L22 OR L23 OR L24 OR L25)
L29	5	SEA FILE=ZCAPLUS ABB=ON PLU=ON L12 OR (L20 OR L21 OR L22 OR L23 OR L24 OR L25 OR L26)

=> d stat que L35
L6 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 8

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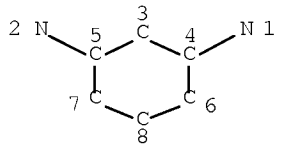
STEREO ATTRIBUTES: NONE
L8          103 SEA FILE=REGISTRY FAM FUL L6
L30           9 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 AND 1/NC
L31         164 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L30
L34       92238 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  ?HYDROCHLORID?/AB,ST,TI
L35           4 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L31 AND L34


=> d stat que L38
L6              STR
```

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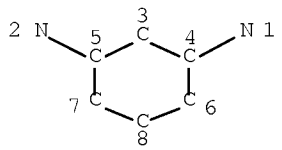
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   8

STEREO ATTRIBUTES: NONE
L8          103 SEA FILE=REGISTRY FAM FUL L6
L30           9 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 AND 1/NC
L31         164 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L30
L32      192120 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  ?HYDROCHLORID?/BI
L33          21 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L31 AND L32
L37          17 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  CYCLOHEXANEDIAMINE DIHYDROCHLO
                RID?/BI
L38           1 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L33 AND L37


=> d stat que L40
L6              STR
```

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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   8

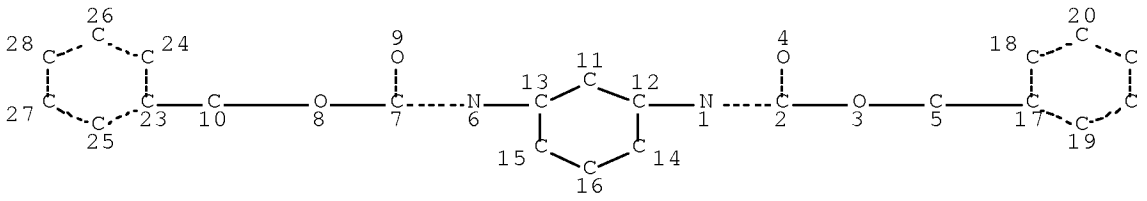
STEREO ATTRIBUTES: NONE
L8          103 SEA FILE=REGISTRY FAM FUL L6
```

```
L30           9 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 AND 1/NC
L31         164 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L30
L32      192120 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  ?HYDROCHLORID?/BI
L33          21 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L31 AND L32
L39        9895 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  HYDROCHLORIDES/BI
L40           1 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L39 AND L33


=> d stat que L45
L34       92238 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  ?HYDROCHLORID?/AB,ST,TI
L43           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CYCLOHEXANEDIAMINE/CN
L44         137 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L43
L45           1 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L34 AND L44


=> d stat que L48
L32      192120 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  ?HYDROCHLORID?/BI
L34       92238 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  ?HYDROCHLORID?/AB,ST,TI
L43           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CYCLOHEXANEDIAMINE/CN
L44         137 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L43
L45           1 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L34 AND L44
L47           3 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L32 AND L44
L48           1 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L45 AND L47


=> d stat que L72
L69             STR
```



```
Page 1-A
 22

 21



Page 1-B
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  28

STEREO ATTRIBUTES: NONE
L71           3 SEA FILE=REGISTRY FAM FUL L69
L72           3 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L71
```

```
=> s L29 or L35 or L38 or L40 or L45 or L48 or L72
L77         12 L29 OR L35 OR L38 OR L40 OR L45 OR L48 OR L72

=> file beilstein
FILE 'BEILSTEIN' ENTERED AT 09:49:43 ON 20 FEB 2008
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FILE LAST UPDATED ON January 3, 2008

FILE COVERS 1771 TO 2007.
*** FILE CONTAINS 10.119,480  SUBSTANCES ***

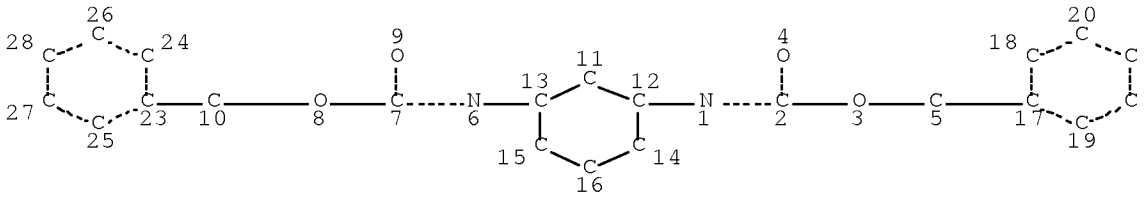
>>>PLEASE NOTE: Reaction Data and substance data are stored in
   separate documents and can not be searched together in one query.
   Reaction data for BEILSTEIN compounds may be displayed
   immediately with the display codes PRE (preparations) and REA
   (reactions).  A substance answer set retrieved after the search
   for a chemical name, a compounds with available reaction
   information by combining with PRE/FA, REA/FA or more generally
   with RX/FA. The BEILSTEIN Registry Number (BRN) is the link
   between a BEILSTEIN compound and belonging reactions. For mo
   detailed reaction searches BRNs can be searched as reaction
   partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE  <<<

*********************************************************************
* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST.               *
* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE  *
* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE         *
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS.                       *
* FOR PRICE INFORMATION SEE HELP COST                               *
*********************************************************************

>>> Price change as of January 1st, 2008: Connect Time and Structure
    Search fees re-introduced. See NEWS and HELP COST <<<

=> d stat que L74
L69             STR
```



Page 1-A

22

21

Page 1-B
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE
L74 2 SEA FILE=BEILSTEIN FAM FUL L69

100.0% PROCESSED 10 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.04

=> file wpix
FILE 'WPIX' ENTERED AT 09:49:59 ON 20 FEB 2008
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FILE LAST UPDATED: 13 FEB 2008 <20080213/UP>
MOST RECENT THOMSON SCIENTIFIC UPDATE: 200811 <200811/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> IPC Reform backfile reclassification has been loaded to the end of November 2007. No update date (UP) has been created for the reclassified documents, but they can be identified by 20060101/UPIC and 20061231/UPIC, 20070601/UPIC, 20071001/UPIC and 20071130/UPIC. <<<

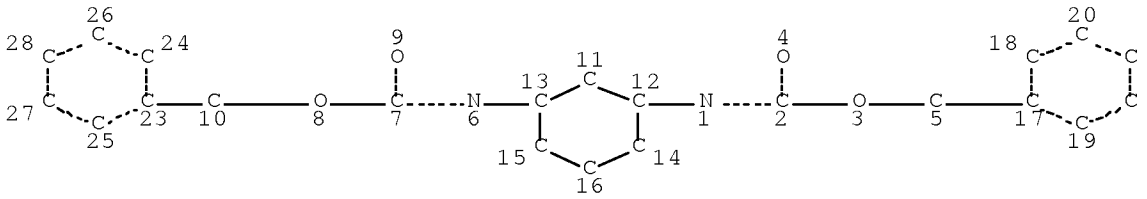
FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

EXPLORE DERWENT WORLD PATENTS INDEX IN STN ANAVIST, VERSION 2.0:
http://www.stn-international.com/archive/presentations/DWPIAnaVist2_0710.pdf

>>> XML document distribution format now available.
See HELP XMLDOC <<<
'BIX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

=> d stat que L76
L69 STR



Page 1-A

22

21

Page 1-B
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE
L76 0 SEA FILE=WPIX FAM FUL L69

100.0% PROCESSED 0 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

=> file uspatfull
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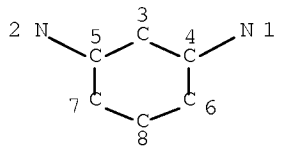
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 19 Feb 2008 (20080219/PD)
FILE LAST UPDATED: 19 Feb 2008 (20080219/ED)
HIGHEST GRANTED PATENT NUMBER: US7334268
HIGHEST APPLICATION PUBLICATION NUMBER: US2008040827
CA INDEXING IS CURRENT THROUGH 19 Feb 2008 (20080219/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 19 Feb 2008 (20080219/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2007
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2007

=> d stat que L50
L6 STR

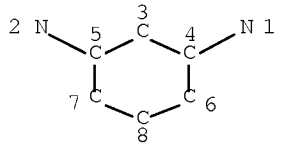


NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 8

```
STEREO ATTRIBUTES: NONE
L8          103 SEA FILE=REGISTRY FAM FUL L6
L10          23 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 AND CL/ELS
L11           4 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 AND ?HYDROCHLORID?/CNS
L50           1 SEA FILE=USPATFULL ABB=ON  PLU=ON  L11


=> d stat que L53
L6              STR
```

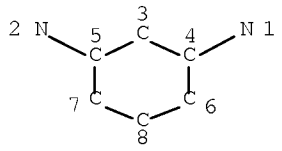



```
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   8

STEREO ATTRIBUTES: NONE
L8          103 SEA FILE=REGISTRY FAM FUL L6
L30           9 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 AND 1/NC
L53          72 SEA FILE=USPATFULL ABB=ON  PLU=ON  L30


=> d stat que L52
L6              STR
```

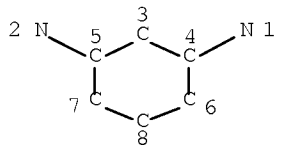



```
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   8

STEREO ATTRIBUTES: NONE
L8          103 SEA FILE=REGISTRY FAM FUL L6
L10          23 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 AND CL/ELS
L11           4 SEA FILE=REGISTRY ABB=ON  PLU=ON  L10 AND ?HYDROCHLORID?/CNS
L50           1 SEA FILE=USPATFULL ABB=ON  PLU=ON  L11
L51      155006 SEA FILE=USPATFULL ABB=ON  PLU=ON  ?HYDROCHLORID?
L52           1 SEA FILE=USPATFULL ABB=ON  PLU=ON  L50 AND L51
```

```
=> d stat que L60
L6              STR
```

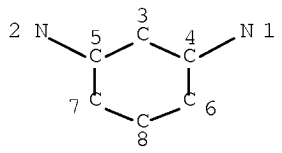



```
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   8

STEREO ATTRIBUTES: NONE
L8           103 SEA FILE=REGISTRY FAM FUL L6
L30            9 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 AND 1/NC
L51       155006 SEA FILE=USPATFULL ABB=ON  PLU=ON  ?HYDROCHLORID?
L53           72 SEA FILE=USPATFULL ABB=ON  PLU=ON  L30
L54           27 SEA FILE=USPATFULL ABB=ON  PLU=ON  L51 AND L53
L55           14 SEA FILE=USPATFULL ABB=ON  PLU=ON  L54 AND PD<20040107
L56           16 SEA FILE=USPATFULL ABB=ON  PLU=ON  L54 AND PRD<20040107
L57           21 SEA FILE=USPATFULL ABB=ON  PLU=ON  L54 AND AD<20040107
L58           23 SEA FILE=USPATFULL ABB=ON  PLU=ON  (L55 OR L56 OR L57)
L59           18 SEA FILE=USPATFULL ABB=ON  PLU=ON  CYCLOHEXANEDIAMINE (10A)
                 ?HYDROCHLORID?
L60            1 SEA FILE=USPATFULL ABB=ON  PLU=ON  L58 AND L59


=> d stat que L58
L6              STR
```




```
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   8

STEREO ATTRIBUTES: NONE
L8           103 SEA FILE=REGISTRY FAM FUL L6
L30            9 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 AND 1/NC
L51       155006 SEA FILE=USPATFULL ABB=ON  PLU=ON  ?HYDROCHLORID?
L53           72 SEA FILE=USPATFULL ABB=ON  PLU=ON  L30
```

```
L54          27 SEA FILE=USPATFULL ABB=ON  PLU=ON  L51 AND L53
L55          14 SEA FILE=USPATFULL ABB=ON  PLU=ON  L54 AND PD<20040107
L56          16 SEA FILE=USPATFULL ABB=ON  PLU=ON  L54 AND PRD<20040107
L57          21 SEA FILE=USPATFULL ABB=ON  PLU=ON  L54 AND AD<20040107
L58          23 SEA FILE=USPATFULL ABB=ON  PLU=ON  (L55 OR L56 OR L57)


=> d stat que L61
L59          18 SEA FILE=USPATFULL ABB=ON  PLU=ON  CYCLOHEXANEDIAMINE (10A)
                ?HYDROCHLORID?
L61           1 SEA FILE=USPATFULL ABB=ON  PLU=ON  1,3 (3W) L59


=> s L50 or L52 or L60 or L58 or L61
L78         24 L50 OR L52 OR L60 OR L58 OR L61

=> file stnguide
FILE 'STNGUIDE' ENTERED AT 09:51:14 ON 20 FEB 2008
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Feb 15, 2008 (20080215/UP).

=> dup rem L77 L74 L76 L78
L76 HAS NO ANSWERS
DUPLICATE IS NOT AVAILABLE IN 'BEILSTEIN'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
FILE 'ZCAPLUS' ENTERED AT 09:51:27 ON 20 FEB 2008
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FILE 'USPATFULL' ENTERED AT 09:51:27 ON 20 FEB 2008
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PROCESSING COMPLETED FOR L77
PROCESSING COMPLETED FOR L74
PROCESSING COMPLETED FOR L76
PROCESSING COMPLETED FOR L78
L79          38 DUP REM L77 L74 L76 L78 (0 DUPLICATES REMOVED)
                ANSWERS '1-12' FROM FILE ZCAPLUS
                ANSWERS '13-14' FROM FILE BEILSTEIN
                ANSWERS '15-38' FROM FILE USPATFULL

=> d ibib abs hitind hitstr L79 1-12; d ide allref L79 13-14; d ibib abs kwic
hitstr L79 15-38

L79  ANSWER 1 OF 38  ZCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2007:7629  ZCAPLUS  Full-text
DOCUMENT NUMBER:          146:106784
TITLE:                    Double para-phenylenediamines joined by a linker
                          comprising a saturated cyclic radical for dyeing of
                          hair
INVENTOR(S):              Sabelle, Stephane; Metais, Eric; Radisson, Xavier
PATENT ASSIGNEE(S):       L'Oreal, Fr.
SOURCE:                   Eur. Pat. Appl., 24pp.
```

CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1739084	A1	20070103	EP 2006-116056	20060626
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
FR 2887878	A1	20070105	FR 2005-51805	20050629
JP 2007008940	A	20070118	JP 2006-178544	20060628
US 2007011825	A1	20070118	US 2006-476816	20060629
PRIORITY APPLN. INFO.:			FR 2005-51805 A	20050629
			US 2005-698935P P	20050714

OTHER SOURCE(S): MARPAT 146:106784

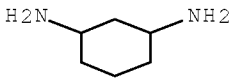
AB Double para-phenylenediamines joined by a linker comprising a saturated cyclic radical are prepared and used for dyeing of hair. Thus, N-(4-aminophenyl)-N-[(3-{[(4-aminophenyl)amino]methyl}cyclohexyl)methyl]am ine tetrahydrochloride (I) was prepared by the hydrogenation of 4-nitro-N-[(3-{[(4-nitrophenyl)amino]methyl}cyclohexyl)methyl]aniline (preparation given) in presence of palladium over carbon. An oxidative hair dye contained I 10-3, benzene-3-ol 10-3, excipients, and water q.s. 100 g. The composition gives an intense gray color to the hair.

CC 62-3 (Essential Oils and Cosmetics)
Section cross-reference(s): 25

IT 350-46-9, Para fluoronitrobenzene 2549-93-1, 1,4-Cyclohexanedimethanamine 2579-20-6, 1,3-Cyclohexanedimethanamine 3385-21-5, 1,3-Cyclohexanediamine 7209-38-3, 1,4-Piperazinedipropanamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(double para-phenylenediamines joined by linker comprising saturated cyclic radical for dyeing of hair)

IT 3385-21-5, 1,3-Cyclohexanediamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(double para-phenylenediamines joined by linker comprising saturated cyclic radical for dyeing of hair)

RN 3385-21-5 ZCAPLUS
CN 1,3-Cyclohexanediamine (CA INDEX NAME)

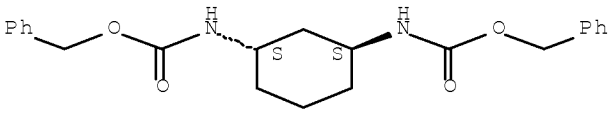


REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 2 OF 38 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:746464 ZCAPLUS Full-text
DOCUMENT NUMBER: 147:314167
TITLE: Discovery of cyclopentane- and cyclohexane-trans-1,3-diamines as potent melanin-concentrating hormone receptor 1 antagonists
AUTHOR(S): Giordanetto, Fabrizio; Karlsson, Olle; Lindberg, Jan;

Larsson, Lars-Olof; Linusson, Anna; Evertsson, Emma; Morgan, David G. A.; Inghardt, Tord
CORPORATE SOURCE: Lead Generation, Computational Chemistry, AstraZeneca R&D Moelndal, Moelndal, SE-431 83, Swed.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2007), 17(15), 4232-4241
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 147:314167
AB The authors herein report the optimization of cyclopentane- and cyclohexane-1,3-diamine derivs. as novel and potent MCH-R1 antagonists. Structural modifications of the 2-amino-quinoline and thiophene moieties found in the initial lead compound served to improve its metabolic stability profile and MCH-R1 affinity, and revealed unprecedented SAR when compared to other 2-amino-quinoline-containing MCH-R1 antagonists.
CC 1-3 (Pharmacology)
Section cross-reference(s): 27
IT 498-62-4, 3-Thiophenecarboxaldehyde 501-53-1 1188-33-6 3385-21-5, 1,3-Cyclohexanediamine 5470-18-8 97892-67-6 860296-78-2 947732-58-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(discovery of cyclopentane- and cyclohexane-trans-1,3-diamines as potent melanin-concentrating hormone receptor 1 antagonists)
IT 860296-78-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(discovery of cyclopentane- and cyclohexane-trans-1,3-diamines as potent melanin-concentrating hormone receptor 1 antagonists)
RN 860296-78-2 ZCAPLUS
CN Carbamic acid, N,N'-(1R,3R)-1,3-cyclohexanediylbis-, C,C'-bis(phenylmethyl) ester, rel- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 3 OF 38 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:940144 ZCAPLUS Full-text
DOCUMENT NUMBER: 145:335693
TITLE: Process for preparation polyisocyanates with solid phosgene
INVENTOR(S): Qiu, Mingjian; Zhang, Wei; Chen, Zhaohui; Zhang, Chunshan; Zhang, Yali
PATENT ASSIGNEE(S): Charna Chemicals Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 7pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1827593	A	20060906	CN 2005-10008982	20050228

PRIORITY APPLN. INFO.: CN 2005-10008982 20050228
OTHER SOURCE(S): CASREACT 145:335693

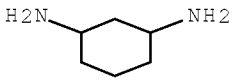
AB This invention provides a process for preparing polyisocyanates comprising reacting solid phosgene with the corresponding polyamines or salts. For example, lysine hydrochloride was reacted with ethanol amine in the presence of hydrochloric acid, followed by the addition of solid phosgene to give lysine triisocyanate with 91.5% purity.

CC 23-18 (Aliphatic Compounds)
Section cross-reference(s): 45

IT 56-40-6, Glycine, reactions 56-85-9, Glutamine, reactions 56-87-1, Lysine, reactions 56-89-3, L-Cystine, reactions 73-22-3, L-Tryptophan, reactions 95-70-5 95-80-7 107-15-3, Ethylene diamine, reactions 110-60-1, 1,4-Butanediamine 124-09-4, 1,6-Hexanediamine, reactions 141-43-5, reactions 591-77-5, 1,4-Pentanediamine 615-71-4, 1,2,4-Benzenetriamine 3114-70-3, 1,4-Diaminocyclohexane 3385-21-5, 1,3-Cyclohexanediamine 7647-01-0D, Hydrochloric acid, compds. with amines 7664-38-2D, Phosphoric acid, compds. with amines 7664-93-9D, Sulfuric acid, compds. with amines 7697-37-2D, Nitric acid, compds. with amines 10098-89-2 32315-10-9, Bis(trichloromethyl) carbonate 66248-00-8 90565-21-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation polyisocyanates with solid phosgene)

IT 3385-21-5, 1,3-Cyclohexanediamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation polyisocyanates with solid phosgene)

RN 3385-21-5 ZCAPLUS
CN 1,3-Cyclohexanediamine (CA INDEX NAME)



L79 ANSWER 4 OF 38 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:696888 ZCAPLUS Full-text
DOCUMENT NUMBER: 143:194018
TITLE: Preparation of substituted diaminoquinazolines as MCH1 receptor ligands for use in the treatment of neurological disorders
INVENTOR(S): Evertsson, Emma; Inghardt, Tord; Lindberg, Jan; Linusson, Anna
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

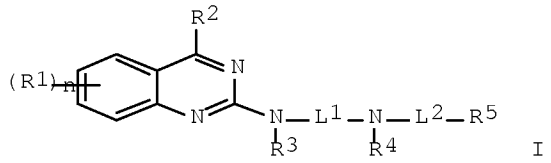
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005070902	A1	20050804	WO 2005-SE10	20050105

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1706388	A1	20061004	EP 2005-704684		20050105
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS					
CN 1906176	A	20070131	CN 2005-80001883		20050105
JP 2007517869	T	20070705	JP 2006-549186		20050105
IN 2006DN03552	A	20070831	IN 2006-DN3552		20060620
US 2007185119	A1	20070809	US 2006-596995		20061122
PRIORITY APPLN. INFO.:			GB 2004-193	A	20040107
			WO 2005-SE10	W	20050105

OTHER SOURCE(S): CASREACT 143:194018; MARPAT 143:194018

GI



I

AB Title compds. I [R1 = alkoxy, alkyl, halo, etc.; n = 0-3; R2 = H, CN, alkyl, etc.; R3 = H, alkyl; L1 = (alkyl)cycloalkyl with provisions; R4 = H, alkyl; L2 = alkylene, etc.; R5 = Ph, naphthyl, heterocyclyl, etc.] are prepared For instance, trans-2-[[3-((benzothiophen-3- yl)amino)cyclohexyl]amino]-4-(dimethylamino)quinazoline is prepared from trans-2-[[3-aminocyclohexyl]amino]-4-(dimethylamino)quinazoline (preparation given) and benzo[b]thiophene-3-carboxaldehyde (MeOH, NaBH3CN). Compds. of the invention exhibit IC50 < 2 μM for the melanin concentrating hormone receptor 1. I are useful in the treatment of obesity, psychiatric disorders, cognitive disorders, memory disorders, schizophrenia, epilepsy, and related conditions, and neurol. disorders such as dementia, multiple sclerosis, Parkinson's disease, Huntington's chorea and Alzheimer's disease and pain related disorders.

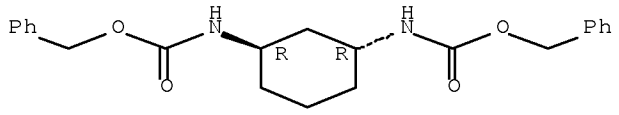
IC ICM C07D239-84
ICS C07D401-12; C07D403-12; C07D409-12; A61K031-517; A61P003-04; A61P025-18; A61P025-28

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT 860296-80-6P 860434-15-7P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted diaminoquinazolines as MCH1 receptor ligands for use in treatment of neurol. disorders)

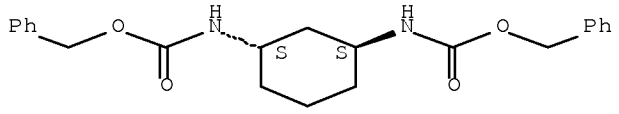
IT 860296-78-2P 860351-60-6P 861846-41-5P 861846-42-6P
861846-43-7P 861846-44-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted diaminoquinazolines as MCH1 receptor ligands for
use in treatment of neurol. disorders)
IT 860296-82-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of substituted diaminoquinazolines as MCH1 receptor ligands for
use in treatment of neurol. disorders)
IT 860296-80-6P 860434-15-7P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted diaminoquinazolines as MCH1 receptor ligands for
use in treatment of neurol. disorders)
RN 860296-80-6 ZCAPLUS
CN Carbamic acid, (1R,3R)-1,3-cyclohexanediylbis-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



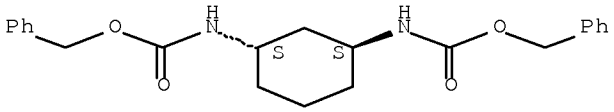
RN 860434-15-7 ZCAPLUS
CN Carbamic acid, (1S,3S)-1,3-cyclohexanediylbis-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



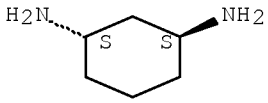
IT 860296-78-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted diaminoquinazolines as MCH1 receptor ligands for
use in treatment of neurol. disorders)
RN 860296-78-2 ZCAPLUS
CN Carbamic acid, N,N'-(1R,3R)-1,3-cyclohexanediylbis-, C,C'-bis(phenylmethyl) ester, rel- (CA INDEX NAME)

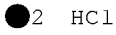
Relative stereochemistry.



IT 860296-82-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of substituted diaminoquinazolines as MCH1 receptor ligands for
use in treatment of neurol. disorders)
RN 860296-82-8 ZCAPLUS
CN 1,3-Cyclohexanediamine, dihydrochloride, (1S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





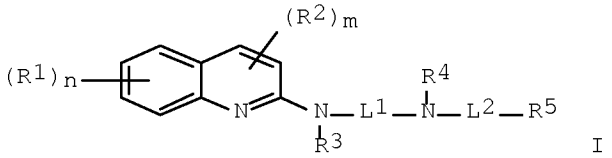
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 5 OF 38 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:638850 ZCAPLUS Full-text
DOCUMENT NUMBER: 143:172772
TITLE: Preparation of quinoline derivatives as MCH modulators
INVENTOR(S): Evertsson, Emma; Inghardt, Tord; Lindberg, Jan; Linusson, Anna; Giordanetto, Fabrizio
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

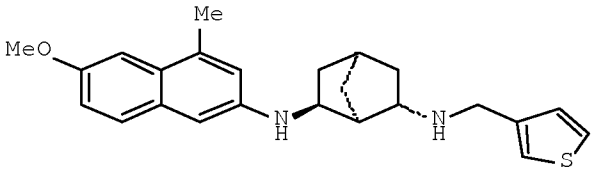
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005066132	A1	20050721	WO 2005-SE4	20050105

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1706384 A1 20061004 EP 2005-704678 20050105
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS
CN 1906169 A 20070131 CN 2005-80001921 20050105
JP 2007517868 T 20070705 JP 2006-549184 20050105
IN 2006DN03548 A 20070817 IN 2006-DN3548 20060620
US 2007185079 A1 20070809 US 2006-596994 20061122
PRIORITY APPLN. INFO.: GB 2004-196 A 20040107
GB 2004-25209 A 20041116
WO 2005-SE4 W 20050105
OTHER SOURCE(S): CASREACT 143:172772; MARPAT 143:172772
GI



I



II

AB Title compds. I [R1 = (un)substituted alkoxy, alkyl, NRaRb, etc.; R2 = (un)substituted alkoxy, alkyl, NRaRb, etc.; Ra and Rb independently = H, alkyl or Ra and Rb together with the nitrogen to which they are attached from a 3-7 membered heterocycle optionally including O; n = 0-3; m = 0-1; R3 = H or alkyl; L1 = (CH2)pcycloalkyl(CH2)q with provisions; p and q independently = 0-1; R4 = H or (un)substituted alkyl; L2 = (un)substituted (CH2)x or 5-6 membered carbocycle fused to R5; x = 1-3; R5 = (un)substituted Ph, naphthyl, heterocycle, etc.] and their pharmaceutically acceptable salts, are prepared and disclosed as melanin concentrating hormone (MCH) modulators. Thus, e.g., II was prepared by palladium catalyzed coupling of benzyl[(1R,2S,4S,6S)-6-aminobicyclo[2.2.1]hept-2- yl]benzylcarbamate (preparation given) with 2-chloro-6-methoxy-4- methylquinoline followed by deprotection and subsequent reductive alkylation with thiophene-3-carbaldehyde. The activity of I was evaluated in MCH1 receptor radioligand binding assays and it was revealed that compds. of the invention displayed IC50 values of less than 2 μM. I as MCH modulator should prove useful in the treatment of obesity, anxiety and depression. Pharmaceutical compns. comprising I are disclosed.

IC ICM C07D215-38
ICS C07D401-12; C07D409-12; C07D417-12; A61K031-47; A61K031-4709; A61P003-04; A61P025-18; A61P025-24; A61P025-28
CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
IT 860296-78-2P

RL: PEP (Physical, engineering or chemical process); PYP (Physical process); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(preparation of quinoline derivs. as MCH modulators)

IT 860296-80-6P
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(preparation of quinoline derivs. as MCH modulators)

IT 79-44-7, Dimethylcarbamyl chloride 90-04-0, o-Anisidine 100-46-9, Benzylamine, reactions 141-82-2, Malonic acid, reactions 141-97-9, Ethyl acetoacetate 147-71-7, D-Tartaric acid 233-88-5, 1H-Pyrrolo[3,2-h]quinoline 271-29-4, 1H-Pyrrolo[2,3-c]pyridine 271-63-6, 1H-Pyrrolo[2,3-b]pyridine 272-49-1, 1H-Pyrrolo[3,2-b]pyridine 274-76-0, Imidazo[1,2-a]pyridine 371-40-4, 4-Fluoroaniline 372-19-0, 3-Fluoroaniline 455-14-1, 4-Aminobenzotrifluoride 498-62-4, Thiophene-3-carbaldehyde 501-53-1, Benzylchloroformate 536-90-3, m-Anisidine 541-41-3, Ethyl chloroformate 542-92-7, Cyclopentadiene, reactions 636-61-3, D(+)-Malic acid 703-61-7, 2,4-Dichloroquinoline 814-68-6, Acryloyl chloride 827-01-0 877-03-2 1192-58-1 1215-59-4, 5-Benzyloxy-1H-indole 1810-72-6, 2,6-Dichloroquinoline 1953-54-4, 1H-Indol-5-ol 2338-71-8 3385-21-5, 1,3-Cyclohexanediamine 3779-27-9, [2,2'-Bithiophene]-5-carboxaldehyde 5467-57-2, 2-Chloroquinoline-4-carboxylic acid 6340-55-2, 2-Chloro-6-methoxy-4-methylquinoline 13669-42-6, Quinoline-3-carbaldehyde 15861-36-6, 1H-Indole-6-carbonitrile 17380-18-6 19012-03-4 27421-51-8 29969-57-1, 2-Chloro-6-nitroquinoline 50634-05-4, 2,5-Dimethoxy-3-tetrahydrofurancarboxaldehyde 50890-83-0, 1-Methyl-1H-indazole-3-carboxylic acid 52606-02-7 79200-56-9, (-)-2-Azabicyclo[2.2.1]hept-5-en-3-one 90723-71-0, 2,6-Dichloro-4-methylquinoline 132706-12-8 175204-81-6 349447-08-1 477848-00-3 477886-95-6 860434-15-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of quinoline derivs. as MCH modulators)

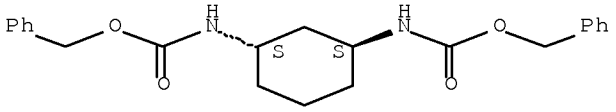
IT 92-15-9P 1578-96-7P 2388-32-1P 4002-83-9P 5652-13-1P 6188-43-8P, Imidazo[1,2-a]pyridine-3-carboxaldehyde 6953-22-6P 10102-94-0P 13523-92-7P 20507-53-3P 25233-47-0P 27257-15-4P 30198-01-7P 40053-37-0P 52173-35-0P 58630-07-2P 67509-84-6P 67999-51-3P 83783-33-9P 89445-80-7P 97892-67-6P 106792-38-5P 131237-81-5P 156496-64-9P 171919-36-1P 238756-47-3P 238756-48-4P 271241-24-8P 271241-25-9P 276862-85-2P 406204-74-8P 441715-30-6P 444683-23-2P 482585-36-4P 645400-43-7P 645400-44-8P 645400-49-3P 645400-50-6P 860296-82-8P 860296-85-1P 860296-97-5P 860297-00-3P 860297-02-5P 860297-04-7P 860297-06-9P 860297-08-1P 860297-09-2P 860297-11-6P 860297-12-7P 860297-13-8P 860297-14-9P 860297-15-0P 860297-16-1P 860297-17-2P 860297-18-3P 860297-19-4P 860297-20-7P 860297-21-8P 860297-22-9P 860297-23-0P 860297-24-1P 860297-25-2P 860297-26-3P 860297-27-4P 860297-28-5P 860297-29-6P 860297-30-9P 860297-31-0P 860297-32-1P 860297-33-2P 860297-34-3P 860297-35-4P 860297-36-5P 860297-37-6P 860297-38-7P 860297-39-8P 860297-40-1P 860297-41-2P 860297-42-3P 860297-43-4P 860297-44-5P 860297-45-6P 860297-46-7P 860297-47-8P 860297-48-9P 860297-49-0P 860297-50-3P 860297-51-4P 860434-14-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinoline derivs. as MCH modulators)

IT 860296-78-2P
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(preparation of quinoline derivs. as MCH modulators)

RN 860296-78-2 ZCAPLUS

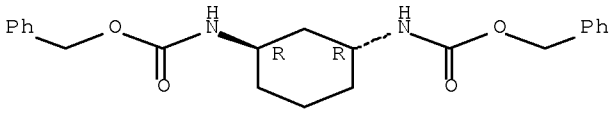
CN Carbamic acid, N,N'-(1R,3R)-1,3-cyclohexanediylbis-, C,C'-bis(phenylmethyl) ester, rel- (CA INDEX NAME)

Relative stereochemistry.



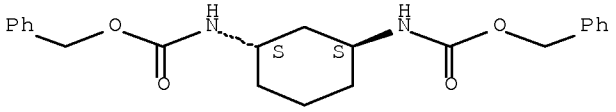
IT 860296-80-6P
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(preparation of quinoline derivs. as MCH modulators)
RN 860296-80-6 ZCAPLUS
CN Carbamic acid, (1R,3R)-1,3-cyclohexanediylbis-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



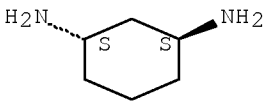
IT 860434-15-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of quinoline derivs. as MCH modulators)
RN 860434-15-7 ZCAPLUS
CN Carbamic acid, (1S,3S)-1,3-cyclohexanediylbis-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 860296-82-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinoline derivs. as MCH modulators)
RN 860296-82-8 ZCAPLUS
CN 1,3-Cyclohexanediamine, dihydrochloride, (1S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

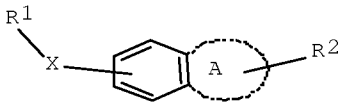
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 6 OF 38 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:964330 ZCAPLUS Full-text
DOCUMENT NUMBER: 138:39295
TITLE: Preparation of heterocyclic compounds as Rho-kinase inhibitors
INVENTOR(S): Imazaki, Naonori; Kitano, Masafumi; Ohashi, Naohito; Matsui, Kazuki
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Company, Limited, Japan
SOURCE: PCT Int. Appl., 425 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002100833	A1	20021219	WO 2002-JP5609	20020606
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002306284	A1	20021223	AU 2002-306284	20020606
EP 1403255	A1	20040331	EP 2002-733352	20020606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004138286	A1	20040715	US 2003-480526	20031212
US 7199147	B2	20070403		

PRIORITY APPLN. INFO.:
JP 2001-176826 A 20010612
JP 2001-398992 A 20011228
WO 2002-JP5609 W 20020606

OTHER SOURCE(S): MARPAT 138:39295
GI



I

AB The title compds. I [wherein one to four groups represented by the general formula R1-X are present and may be the same or different from each other; A is a saturated or unsatd. five-membered heterocycle; X is a single bond, N(R3), O, S, or the like; R1 is hydrogen, halogeno, nitro, carboxyl, substituted or unsubstituted alkyl, or the like; R2 is hydrogen, halogeno, nitro, carboxyl, substituted or unsubstituted alkyl, or the like; and R3 is hydrogen, substituted or unsubstituted alkyl, or the like] are prepared N-(1-Benzyl-4-piperidinyl)-1H-indazole-5-amine dihydrochloride monohydrate in vitro showed IC50 of 0.4 μL/mL against Rho-kinase.

IC ICM C07D231-56
ICS A61K031-416; A61K031-453; A61K031-4535; A61K031-454; A61K031-46; A61P009-00; A61P009-10; A61P009-12; A61P013-02; A61P013-12; A61P015-00; A61P015-08; A61P019-08; A61P025-28; A61P027-02; A61P027-06; A61P029-00; A61P031-04; A61P031-18

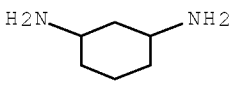
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT 50-00-0, Formalin, reactions 62-23-7, p-Nitrobenzoic acid 64-19-7, Acetic acid, reactions 67-64-1, Acetone, reactions 70-54-2, Lysine 74-88-4, Methyl iodide, reactions 74-89-5, Methylamine, reactions 75-36-5, Acetyl chloride 75-65-0, tert-Butanol, reactions 76-83-5, Triphenylmethyl chloride 78-81-9, Isobutylamine 79-04-9, Chloroacetyl chloride 79-09-4, Propionic acid, reactions 79-14-1, Hydroxyacetic acid, reactions 79-22-1, Methyl chloroformate 79-31-2, Isobutyric acid 80-62-6, Methyl methacrylate 85-41-6, Phthalimide 89-98-5, 2-Chlorobenzaldehyde 95-23-8 96-33-3, Methyl acrylate 96-41-3, Cyclopentanol 99-65-0, m-Dinitrobenzene 100-39-0, Benzyl bromide 100-44-7, Benzyl chloride, reactions 100-46-9, N-Benzylamine, reactions 100-52-7, Benzaldehyde, reactions 102-50-1, 4-Methoxy-2-methylaniline 103-49-1, Dibenzylamine 103-63-9, Phenethyl bromide 103-67-3, N-Benzylmethylamine 105-39-5, Chloroacetic acid ethyl ester 106-94-5, n-Propyl bromide 107-08-4, Propyl iodide 107-30-2, Chloromethyl methyl ether 108-24-7, Acetic anhydride 108-30-5, Succinic anhydride, reactions 108-68-9, 3,5-Dimethylphenol 108-86-1, Bromobenzene, reactions 108-93-0, Cyclohexanol, reactions 110-52-1, 1,4-Dibromobutane 110-87-2, 3,4-Dihydro-2H-pyran 110-91-8, Morpholine, reactions 111-30-8, Glutaraldehyde 119-36-8, Salicylic acid methyl ester 123-38-6, Propionaldehyde, reactions 124-40-3, Dimethylamine, reactions 124-63-0, Methanesulfonyl chloride 143-33-9, Sodium cyanide 151-50-8, Potassium cyanide 350-30-1, 3-Chloro-4-fluoronitrobenzene 350-46-9, 4-Fluoronitrobenzene 358-23-6, Trifluoromethanesulfonic anhydride 407-25-0, Trifluoroacetic anhydride 446-33-3, 5-Fluoro-2-nitrotoluene 506-59-2, Dimethylamine hydrochloride 515-74-2, Sodium sulfanilate 540-51-2, 2-Bromoethanol 556-48-9, 1,4-Cyclohexanediol 577-19-5, 2-Bromonitrobenzene 589-10-6, 2-Phenoxyethyl bromide 591-97-9, 1-Chloro-2-butene 615-53-2, N-Methyl-N-nitrosourethane 619-24-9, 3-Nitrobenzonitrile 624-76-0, 2-Iodoethanol 625-36-5, 3-Chloropropionyl chloride 626-88-0, 1-Bromo-4-methylpentane 646-07-1, 4-Methylvaleric acid 654-76-2, 2-Methoxy-5-nitrobenzotrifluoride 697-82-5, 2,3,5-Trimethylphenol 872-85-5, Isonicotinaldehyde 930-68-7, 2-Cyclohexen-1-one 934-22-5,

1H-Benzimidazol-5-amine 1072-72-6, Tetrahydrothiopyran-4-one 1073-13-8, 4,4-Dimethyl-2-cyclohexen-1-one 1194-02-1, 4-Fluorobenzonitrile 1759-53-1, Cyclopropanecarboxylic acid 2081-44-9, 4-Hydroxytetrahydropyran 2201-24-3, 1-Phenylcyclohexylamine 2615-25-0, trans-1,4-Diaminocyclohexane 2759-28-6, 1-Benzylpiperazine 3096-69-3, 2,3-Dimethyl-4-aminophenol 3251-56-7, 2-Methoxy-4-nitrophenol 3282-30-2, Pivaloyl chloride 3385-21-5, 1,3-Diaminocyclohexane 3612-20-2, 1-Benzyl-4-piperidone 4376-18-5, Phthalic acid monomethyl ester 4635-59-0, 4-Chlorobutyryl chloride 4908-50-3 5006-62-2, Ethyl 3-piperidinecarboxylate 5401-94-5, 5-Nitroindazole 5414-19-7, Bis(2-bromoethyl) ether 5460-31-1, 3-Nitro-o-cresol 6051-66-7, 2,5-Dimethylterephthalic acid 6436-90-4, N-Benzylglycine ethyl ester 6482-24-2, 2-Bromoethyl methyl ether 6859-99-0, 3-Hydroxypiperidine 6936-47-6, cis-2-Aminocyclohexanol hydrochloride 6967-12-0, 1H-Indazol-6-amine 7486-35-3, Tributylvinyltin 7664-41-7, Ammonia, reactions 7803-49-8, Hydroxylamine, reactions 10315-07-8, 1-Benzyl-4-piperidinecarboxylic acid 13139-17-8, 1-[[(Benzyloxy)carbonyl]oxy]-2,5-pyrrolidinedione 14660-52-7, Ethyl 5-bromovalerate 17159-80-7, Ethyl 4-hydroxycyclohexanecarboxylate 17449-76-2, Methyl 4-hydroxycyclohexanecarboxylate 18162-48-6, tert-Butyldimethylsilyl chloride 18595-14-7, Methyl 4-amino-3-methylbenzoate 19335-11-6, 5-Aminoindazole 19438-10-9, 3-Hydroxybenzoic acid methyl ester 19499-93-5, 2,3-Dimethyl-4-nitrophenol 22509-74-6, N-Carboethoxyphthalimide 24424-99-5, Di-tert-butyl dicarbonate 25912-50-9, 3-Aminocyclohexanecarboxylic acid 26386-88-9, Diphenylphosphoryl azide 27489-62-9, trans-4-Aminocyclohexanol 30525-89-4, Paraformaldehyde 33024-60-1, Tetrahydro-2H-pyran-4-ylamine monohydrochloride 50593-24-3, 1-Methyl-1H-indazol-5-amine 51535-00-3, Methyl 1-benzyl-5-oxo-3-pyrrolidinecarboxylate 53857-57-1, 5-Bromo-1H-indazole 54288-70-9, 4-Bromopiperidine hydrobromide 59247-47-1, tert-Butyl-4-bromobenzoate 59719-74-3, 1,3-Cyclopentanediol 60206-30-6, 8-Propyl-8-azabicyclo[3.2.1]octan-3-one 60518-59-4, 2-Methyl-2H-indazol-5-amine 63301-31-5 74626-47-4, 1H-Indazole-5-carbonitrile 76445-65-3, 4-Aminocyclohexanol hydrochloride 81029-03-0, 2,3-Dimethyl-4-nitroanisole 84358-13-4, 1-(tert-Butoxycarbonyl)-4-piperidinecarboxylic acid 97181-50-5 99799-10-7 103057-44-9, tert-Butyl 3-hydroxypyrrolidine-1-carboxylate 109384-19-2, tert-Butyl 4-hydroxypiperidine-1-carboxylate 132302-53-5, 2-(1H-Indazol-5-ylamino)benzoic acid 215120-68-6, 4-([[(Benzyloxy)carbonyl]amino]methyl) cyclohexanecarboxylic acid 239097-74-6, 1,2-Benzisoxazol-5-amine 248924-30-3 261762-91-8 280772-00-1, 1-(Methylsulfonyl)-4-piperidinecarboxylic acid 478841-81-5 478920-45-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heterocyclic compds. as Rho-kinase inhibitors)

IT 3385-21-5, 1,3-Diaminocyclohexane
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heterocyclic compds. as Rho-kinase inhibitors)

RN 3385-21-5 ZCAPLUS
CN 1,3-Cyclohexanediamine (CA INDEX NAME)



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 7 OF 38 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:876479 ZCAPLUS Full-text
DOCUMENT NUMBER: 138:197750
TITLE: Insights into the van der Waals radius of low-spin Ni(II) from molecular mechanics studies and the crystal structures of [Ni(cis-cyclohexane-1,3-diamine)2]Cl2, [Ni{(R)-5,5,7-trimethyl-1,4-diazacycloheptane}2]Cl2·H2O and [Ni(5,7-dimethyl-1,4-diazacycloheptane)2](ClO4)2. Synthesis of 5,7-dimethyl-1,4-diazacycloheptane and an improved synthesis of cis-cyclohexane-1,3-diamine
AUTHOR(S): Munk, Vivienne P.; Cham, S. Tsuey; Fenton, Ronald R.; Hocking, Rosalie K.; Hambley, Trevor W.
CORPORATE SOURCE: Centre for Heavy Metals Research, School of Chemistry, University of Sydney, Sydney, N.S.W. 2006, Australia
SOURCE: Australian Journal of Chemistry (2002), 55(8), 523-529
CODEN: AJCHAS; ISSN: 0004-9425
PUBLISHER: CSIRO Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:197750

AB The structures of three bis(diamine)nickel(II) complexes, chosen to shed light on the van der Waals radius of Ni(II), are described. [Ni(cis-1,3-chxn)2]Cl2 (cis-1,3-chxn = cis-cyclohexane-1,3-diamine) crystallizes in the monoclinic space group P21/n, with a 6.397(2), b 16.463(4), c 7.229(2) Å, b 90.70(2)°, and its structure was refined to an R value of 0.031 on 1214F. [Ni{(R)-tmdz}2]Cl2·H2O (tmdz = 5,5,7-trimethyl-1,4-diazacycloheptane) crystallizes in the orthorhombic space group P212121, with a 10.678(1), b 11.073(5), c 17.968(6) Å, and its structure was refined to an R value of 0.031 on 1586F. [Ni(dmdz)2](ClO4)2 (dmdz = 5,7-dimethyl-1,4-diazacycloheptane) crystallizes in the monoclinic space group P21/n, with a 9.582(1), b 10.390(2), c 11.817(3) Å, β 96.19(2)°, and its structure was refined to an R value of 0.059 on 817F. In all three structures, short Ni...H and Ni...C interactions, ranging from 2.37 to 2.61 Å and 2.99 to 3.03 Å, resp., are observed Using mol. mechanics modeling to reproduce these sepns., the authors have arrived at a van der Waals radius of 1.35 Å for low-spin Ni(II). Anal. of Ni...O contacts in the solid state leads to a van der Waals radius of .apprx.1.26 Å, which is consistent with the mol. mechanics-derived value since these are usually longer. Cyclohexane-1,3-diamine was prepared via the Schmidt reaction of cyclohexane-1,3-dicarboxylic acid (NaN3 and H2SO4 in CHCl3, then base hydrolysis). Dmdz was prepared via cyclization of pent-3-en-2-one with ethane-1,2-diamine, followed by reduction of the diimine with NaBH4.

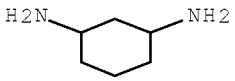
CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 65, 75

IT 3385-21-5P, 1,3-Cyclohexanediamine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and resolution via selective complexation of nickel(II) with cis isomer)

IT 32189-21-2P, trans-N,N'-Diacetylcyclohexane-1,3-diamine
RL: PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PYP (Physical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(preparation and separation from cis isomer via crystallization)

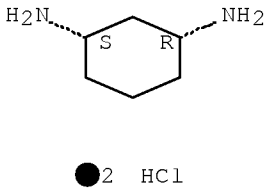
IT 498532-32-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation from free base)

IT 498532-29-9P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, acid hydrolysis to give cyclohexanediamine dihydrochloride, and crystal structure in relation to van der Waals radius of low-spin Ni(II))
IT 32189-20-1P, cis-N,N'-Diacetylcyclohexane-1,3-diamine
RL: PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PYP (Physical process); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(preparation, separation from trans isomer via crystallization, and conversion
to dihydrochloride)
IT 3385-21-5P, 1,3-Cyclohexanediamine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and resolution via selective complexation of nickel(II) with cis isomer)
RN 3385-21-5 ZCAPLUS
CN 1,3-Cyclohexanediamine (CA INDEX NAME)



IT 498532-32-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation from free base)
RN 498532-32-4 ZCAPLUS
CN 1,3-Cyclohexanediamine, dihydrochloride, (1R,3S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

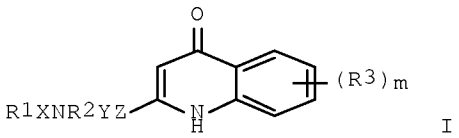
L79 ANSWER 8 OF 38 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:708742 ZCAPLUS Full-text
DOCUMENT NUMBER: 131:322546
TITLE: Preparation of 2-aminoquinolin-4-ones as inhibitors of methionyl tRNA synthase.
INVENTOR(S): Berge, John Michael; Brown, Pamela; Elder, John Stephen; Forrest, Andrew Keith; Hamprecht, Dieter

Wolfgang; Jarvest, Richard Lewis; Mcnair, David Jonathan; Sheppard, Robert John
PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9955677	A1	19991104	WO 1999-EP2648		19990415
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2330564	A1	19991104	CA 1999-2330564		19990415
AU 9935235	A	19991116	AU 1999-35235		19990415
BR 9909994	A	20001226	BR 1999-9994		19990415
TR 200003170	T2	20010122	TR 2000-3170		19990415
EP 1084110	A1	20010321	EP 1999-916927		19990415
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI					
HU 2001003093	A2	20020228	HU 2001-3093		19990415
HU 2001003093	A3	20020328			
JP 2002513005	T	20020508	JP 2000-545837		19990415
ZA 2000005781	A	20010604	ZA 2000-5781		20001018
NO 2000005400	A	20001026	NO 2000-5400		20001026
MX 2000PA10551	A	20010507	MX 2000-PA10551		20001026
US 6320051	B1	20011120	US 2000-674102		20001026
PRIORITY APPLN. INFO.:			GB 1998-9050	A	19980429
			GB 1998-24571	A	19981109
			WO 1999-EP2648	W	19990415

OTHER SOURCE(S): MARPAT 131:322546

GI



I

AB Title compds. [I; R1 = (substituted) aryl, heteroaryl; R2 = H, alkyl, aralkyl, aralkenyl, alkylcarbonyl; R3 = halo, cyano, OH, (substituted) alkyl, cycloalkyl, alkoxy, amino, acylamino, CO2H, etc.; X = CHR4, alkylene, alkenylene, CO; R4 = H, alkyl, aryl; Y = (substituted) alkylene, etc.; Z = NH, O; R1X or R1R2 = (substituted) alkylene; XR2, XY, or YR2 = atoms to form a 4-7 membered ring; m = 0-3], were prepared Thus, 2-chloro-4-ethoxyquinoline and 1,3-diaminopropane were heated at 60° for 48 h to give 77% 2-(3-aminoprop-1-

ylamino)-4- ethoxyquinoline. This was refluxed with concentrate HCl for 24 h to give 100% 2-(3-aminoprop-1-ylamino)-1H-quinolin-4-one dihydrochloride. The latter was stirred 40 min. with quinoline-3-carboxaldehyde and NaOAc in DMF/HOAc; Na(OAc)3BH was added and the mixture was stirred 2 h to give 2-[3-(3-quinolylmethylamino)prop-1-ylamino]-1H-quinolin-4-one. I inhibited S. aureus methionyl tRNA synthase with IC50's of <3nM to 700 nM.

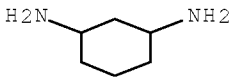
IC ICM C07D215-38
ICS A61K031-47; C07D405-12; C07D401-12; C07D409-12

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

IT 51-44-5, 3,4-Dichlorobenzoic acid 66-99-9, Naphthalene-2-carboxaldehyde 67-64-1, 2-Propanone, reactions 87-61-6, 1,2,3-Trichlorobenzene 90-60-8, 3,5-Dichlorosalicylaldehyde 96-48-0 102-47-6, 3,4-Dichlorobenzyl chloride 103-63-9, (2-Bromoethyl)benzene 105-07-7, 4-Cyanobenzaldehyde 106-49-0, 4-Methylaniline, reactions 107-15-3, 1,2-Ethanediamine, reactions 108-42-9, 3-Chloroaniline 109-76-2, 1,3-Diaminopropane 110-60-1, 1,4-Butanediamine 141-82-2, Malonic acid, reactions 156-87-6 447-61-0, 2-Trifluoromethylbenzaldehyde 459-57-4, 4-Fluorobenzaldehyde 462-94-2, 1,5-Diaminopentane 541-73-1, 1,3-Dichlorobenzene 579-18-0, 3-Benzoylbenzoic acid 587-04-2, 3-Chlorobenzaldehyde 696-41-3, 3-Iodobenzaldehyde 703-61-7, 2,4-Dichloroquinoline 1189-71-5, Chlorosulfonyl isocyanate 2039-83-0, 3,4-Dichlorostyrene 2433-85-4, 4,5-Dibromofuran-2-carboxaldehyde 2642-63-9 2706-56-1, 2-Pyridineethanamine 3279-81-0, 4-Chloro-3-sulfamoylbenzaldehyde 3385-21-5, 1,3-Diaminocyclohexane 3456-99-3 4265-16-1, Benzofuran-2-carboxaldehyde 4295-08-3, 2-Chloro-4-ethoxyquinoline 4295-09-4, 2-Chloro-4-methoxyquinoline 5896-17-3, 2-Benzyloxybenzaldehyde 6284-79-3, 3,4-Dichlorobenzophenone 6287-38-3, 3,4-Dichlorobenzaldehyde 7254-19-5, 5-Bromoindole-2-carboxylic acid 7687-79-8 10203-08-4, 3,5-Dichlorobenzaldehyde 10465-81-3 13669-42-6, Quinoline-3-carboxaldehyde 14371-10-9, trans-Cinnamaldehyde 17352-25-9, 3,5-Diiodobenzaldehyde 18880-04-1, 3,4-Dichlorobenzyl bromide 22031-52-3, 6-Azabicyclo[3.2.0]heptan-7-one 24680-50-0 34328-46-6, 4-Chloro-3-trifluoromethylbenzaldehyde 34328-61-5, 3-Chloro-4-fluorobenzaldehyde 38071-22-6, 4,5-Dibromothiophene-2-carboxaldehyde 38091-73-5 40359-57-7, 2-Benzyloxy-3,5-dichlorobenzaldehyde 41365-75-7 41667-95-2, 5,6-Dichloronicotinic acid 50910-55-9, 2-Amino-3,5-dibromobenzaldehyde 52176-31-5, 2-Amino-4-ethoxyquinoline 53995-82-7 55144-92-8, 3-(2,4-Dichlorophenyl)propanoic acid 56123-06-9, 2-Methylenepropane-1,3-diamine 56961-75-2, 2,3,5-Trichlorobenzaldehyde 56990-02-4, 3,5-Dibromobenzaldehyde 60125-24-8, trans-2-Methoxycinnamaldehyde 61657-67-8, 3,5-Dibromo-2-ethoxybenzaldehyde 74896-66-5 93467-56-2 102000-64-6 149877-00-9 151379-87-2 158414-41-6 181280-06-8 248607-95-6 248607-96-7 248607-97-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-aminoquinolin-4-ones as inhibitors of methionyl tRNA synthase)

IT 3385-21-5, 1,3-Diaminocyclohexane
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-aminoquinolin-4-ones as inhibitors of methionyl tRNA synthase)

RN 3385-21-5 ZCAPLUS
CN 1,3-Cyclohexanediamine (CA INDEX NAME)



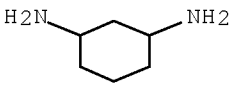
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 9 OF 38 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1970:466129 ZCAPLUS Full-text
DOCUMENT NUMBER: 73:66129
ORIGINAL REFERENCE NO.: 73:10823a,10826a
TITLE: Hydrogenation of phenylprimary amines to cyclohexyl amines
INVENTOR(S): Greco, Nicholas P.
PATENT ASSIGNEE(S): Koppers Co., Inc.
SOURCE: U.S., 3 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3520928	A	19700721	US 1967-663235	19670825
PRIORITY APPLN. INFO.:			US 1967-663235 A	19670825

AB The mineral acid salts of aromatic primary amines were hydrogenated in aqueous solution in the presence of Pt or Pd catalyst. o-Aminophenol sulfate (0.93 mole) formed by addition of equimolar amts. of o-H2NC6H4OH and H2SO4, in 500 ml H2O was hydrogenated in a N purged autoclave over 1 g Pt at 55°/200 psig. After 20 min reaction time the catalyst was removed, the aqueous solution alkalized with NaOH, and extracted with Et2O to give 90% 2-aminocyclohexanol (a mixture of stereoisomers), b23 82-123°. Also prepared were: 1,4- and 1,3-diaminocyclohexane, di-HCl salts in 100 and 96% yields resp.; 4-methylcyclohexylamine and cyclohexylamine in 95 and 97% yields resp.; and 2,4- and 2,6-diamino-methylcyclohexanes in 97 and 98% yields resp. These compds. are useful in producing urethanes.

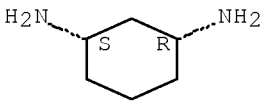
IC C07B; C07C
INCL 260563000
CC 24 (Alicyclic Compounds)
IT 931-15-7P 6321-23-9P 6982-39-4P 13897-55-7P 13897-56-8P
28294-92-0P 28294-93-1P 28294-95-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
IT 28294-92-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 28294-92-0 ZCAPLUS
CN 1,3-Cyclohexanediamine, dihydrochloride (8CI) (CA INDEX NAME)

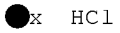


●2 HCl

L79 ANSWER 10 OF 38 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1971:87470 ZCAPLUS Full-text
DOCUMENT NUMBER: 74:87470
ORIGINAL REFERENCE NO.: 74:14193a,14196a
TITLE: Separation and analysis of geometric isomers of 1,3- and 1,4-diaminocyclohexanes
AUTHOR(S): Kozhevov, A. G.; Genkina, E. V.; Usova, E. R.; Shmidt, Ya. A.
CORPORATE SOURCE: Gos. Inst. Azotn. Prom. Prod. Org. Sin., Moscow, USSR
SOURCE: Zhurnal Vsesoyuznogo Khimicheskogo Obshchestva im. D. I. Mendeleeva (1970), 15(4), 456-7
CODEN: ZVKOA6; ISSN: 0373-0247
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB A mixture of 1,3-diaminocyclohexane (I) isomers was determined, by gas chromatog. over polyethylene glycol at 210°, to be 65.5 cis-I and 34.5 trans-I. I and Ac2O gave the diamide mixture which was separated into the cis- and trans-diamides. Treatment of the pure diamides 14 hr with HCl gave cis-I and trans-I. A mixture of 1,4-diaminocyclohexane (II) isomers contained 76 cis-II and 24 trans-II. The II isomers were separated as their di-Me dicarbamates (from MeO2CCl) which were hydrolyzed 25 hr in HCl to give the pure II isomers.
CC 24 (Alicyclic Compounds)
ST amino cyclohexanes isomers analysis; cyclohexanes isomers analysis amino; sepn amino cyclohexanes isomers
IT 2615-25-0P 15827-56-2P 26772-34-9P 26883-70-5P 32175-26-1P 32175-29-4P 32175-30-7P 32189-20-1P 32189-21-2P 32222-08-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
IT 32175-26-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 32175-26-1 ZCAPLUS
CN 1,3-Cyclohexanediamine, hydrochloride, cis- (8CI) (CA INDEX NAME)

Relative stereochemistry.





L79 ANSWER 11 OF 38 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1959:6638 ZCAPLUS Full-text
DOCUMENT NUMBER: 53:6638
ORIGINAL REFERENCE NO.: 53:1181g-i,1182a-c
TITLE: N-Bis(chloroethyl)amines of alicyclic series I
AUTHOR(S): Sergievskaya, S. I.; Levshina, K. V.; Chizhov, A. K.; Gavrilova, A. I.; Kravchenko, A. I.
CORPORATE SOURCE: S. Ordzhonikidze All-Union Chem. Pharm. Research Inst., Moscow
SOURCE: Zhurnal Obshchei Khimii (1958), 28, 1839-45

CODEN: ZOKHA4; ISSN: 0044-460X
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 53:6638

AB cf. C.A. 53, 1196g. The following compds. were prepared as a part of the anticancer research program; a preliminary report on biol. activity describes the N-(dichloroalkyl)amines of the cycloheptane group as the most active and least toxic of the series. Hydrogenation of Et p-aminobenzoate over Pt at 50 atmospheric and room temperature gave Et p-aminocyclohexanecarboxylate, b20-3 125-35°, also prepared in 45% yield from the acid and alc. HCl; the pure ester, b20 125°, n20D 1.4640. Hydrogenation of m-aminobenzoic acid gave m-aminocyclohexanecarboxylic acid, m. 251-2°, which with alc. HCl gave 75% Et ester, b15 120-5°, n20D 1.4640. Hydrogenation of m-phenylenediamine-2HCl over Pt gave, after treatment of the crude product with hot aqueous CaO, a low yield of m-cyclohexylene-diamine, b30 97°, n20.5D 1.5205. Hydrogenation of cycloheptanone in MeOH over Raney Ni gave cycloheptanol, b1279-82°. RMgCl from chlorocycloheptane and CH2O gave after the usual treatment cycloheptylcarbinol, b8-9 84-9°, which with SOCl2 in CHCl3 gave (chloromethyl)cycloheptane, b8-10 62-72°. This with an equimolar amount of diethanolamine and Et3N in a sealed tube 8-9 hrs. at 200° gave the desired bis(2-hydroxyethyl)amines, also formed from the alicyclic amine and 2 moles ethylene oxide at 120-40°. The hydroxyethyl derivs. were treated 8 hrs. with 6 moles SOCl2 in CHCl3 yielding the desired chloroethyl analogs. Thus were obtained the following RN(CH2CH2OH)2 (R and b.p. given): C5H9, b6 152-4°; C6H11, b15 150°; C6H10(CO2Et)-p, b0.25 166-6.5°; C6H10(CO2Et)-m, b4 170-5°; C7H13, b4 173-83°. R[N(CH2CH2OH)2]2: m-C6H10, b11 252-4°. RN(CH2CH2Cl)2.HCl: C5H9, m. 106-7°; C6H11, m. 175-6°; p-EtO2CC6H10, m. 175-6°; m-isomer, m. 133-5°; p-HO2CC6H10, m. 157-60°; m-isomer, decompose 68°; C7H13, m. 178°; C5H9CH2, m. 128-30°; C6H11CH2, m. 145-7°; C7H13CH2, m. 141-3°. m- C6H10[N(CH2CH2Cl)2]2. -2HCl, m. 101°. The substituted cyclohexanecarboxylic acids were best prepared by saponification of the Et esters with concentrated HCl.

CC 10D (Organic Chemistry: Alicyclic Compounds)

IT 740047-74-9, Cyclohexanecarboxylic acid, 4-[bis(2-chloroethyl)amino]-
807265-70-9, Cyclohexanecarboxylic acid, 3-[bis(2-chloroethyl)amino]-
(hydrochlorides, and Et esters)

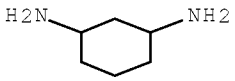
IT 3385-21-5P, 1,3-Cyclohexanediamine
RL: PREP (Preparation)
(preparation from m-phenylenediamine)

IT 879-61-8P, Cyclohexylamine, N,N-bis(2-chloroethyl)-, hydrochloride
4500-29-2P, Ethanol, 2,2'-(cyclohexylimino)di- 57156-26-0P,
Cycloheptylamine, N,N-bis(2-chloroethyl)-, hydrochloride
91139-09-2P, Cyclopentanemethylamine, N,N-bis(2-chloroethyl)-,
hydrochloride 92244-83-2P, Cyclohexanemethylamine,
N,N-bis(2-chloroethyl)-, hydrochloride 98956-90-2P, Ethanol,
2,2'-(cyclopentylimino)di- 99064-52-5P, Cyclopentylamine,
N,N-bis(2-chloroethyl)-, hydrochloride 99969-52-5P,
Cycloheptane, (chloromethyl)- 100246-80-8P, Cycloheptanemethylamine,
N,N-bis(2-chloroethyl)-, hydrochloride 100387-25-5P, Ethanol,
2,2'-(cycloheptylmethylimino)di- 100535-48-6P, Ethanol,
2,2'-(cycloheptylimino)di- 106783-33-9P, 1,3-Cyclohexanediamine,
N,N,N',N'-tetrakis(2-chloroethyl)-, dihydrochloride
110062-37-8P, Ethanol, 2,2',2'',2'''-(1,3-cyclohexylenedinitrilo)tetra-
RL: PREP (Preparation)
(preparation of)

IT 3385-21-5P, 1,3-Cyclohexanediamine
RL: PREP (Preparation)
(preparation from m-phenylenediamine)

RN 3385-21-5 ZCAPLUS

CN 1,3-Cyclohexanediamine (CA INDEX NAME)



L79 ANSWER 12 OF 38 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1956:67486 ZCAPLUS Full-text
DOCUMENT NUMBER: 50:67486
ORIGINAL REFERENCE NO.: 50:12548d-g
TITLE: Polyurethans
PATENT ASSIGNEE(S): Badische Anilin- & Soda-Fabrik Akt.-Ges.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 743917		19560125	GB 1953-7582	19530319

AB Cross-linked polyurethans are prepared by reaction of a bischlorocarbonic acid ester (I) and a diamine in the presence of one or more compds. containing 3 or 4 primary or secondary amino groups and (or) in the presence of one or more tri- or tetracarbonic acid esters. The total number of amino groups is equivalent to the total number of I groups. The reaction mixture contains, for each functional group forming part of a bifunctional reactant, 0.01-0.05 part of a functional group forming part of a tri- or tetrafunctional reactant. Thus, 21.5 parts 1,4-butanediol bis-(chlorocarbonic acid) ester and 0.2 part tris(hydroxymethyl)propane tris(chlorocarbonic acid) ester dissolved in 80 parts C6H6 were emulsified with 18 parts hexamethylenediamine-dihydrochloride in 40 parts water with addition of 2 parts polyglycol ether of dodecyl alc. The emulsion was allowed to flow in a thin stream at 5-20° into a solution of 17 parts NaOH in 150 parts water. It was allowed to react further for 1 hr. at room temperature and then for 1 hr. at 50°. C6H6 was expelled by steam distillation The polyurethan formed was filtered, washed, and dried. It was a fine, white powder m. >180° and suitable for injection molding and for stiff bristles. Cf. C.A. 47, 5169a; following abstract

CC 31 (Synthetic Resins and Plastics)

IT 56-18-8, Dipropylamine, 3,3'-diamino- 1761-71-3, Cyclohexylamine, 4,4'-methylenebis- 19475-66-2, 1,6-Hexanediamine, N-(3-aminopropyl)- 26650-11-3, 1,6-Hexanediamine, N,N'-bis(3-aminopropyl)- 29256-90-4, Cyclohexanediamine
(cross-linked polyurethans from)

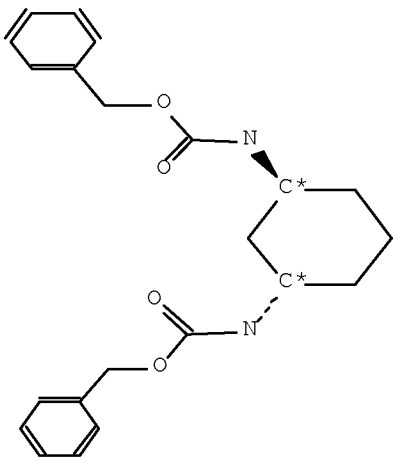
IT 29256-90-4, Cyclohexanediamine
(cross-linked polyurethans from)

RN 29256-90-4 ZCAPLUS
CN Cyclohexanediamine (CA INDEX NAME)

2 [D1—NH2]

L79 ANSWER 13 OF 38 BEILSTEIN COPYRIGHT 2008 BEILSTEIN MDL on STN

Beilstein Records (BRN):	3223185
Chemical Name (CN):	N,N'-(trans-cyclohexane-1,3-diyl)-bis-carbamic acid dibenzyl ester
Autonom Name (AUN):	(3-benzyloxycarbonylamino-cyclohexyl)-carbamic acid benzyl ester
Molec. Formula (MF):	C22 H26 N2 O4
Molecular Weight (MW):	382.46
Lawson Number (LN):	14460, 5228, 1762
File Segment (FS):	racemate, Stereo compound
Compound Type (CTYPE):	isocyclic
Constitution ID (CONSID):	2951475
Tautomer ID (TAUTID):	3156780
Beilstein Citation (BSO):	4-13-00-00011
Entry Date (DED):	1990/02/15
Update Date (DUPD):	1990/02/15



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Additionally represents mirror image
Stereo Descriptor: +/-

Field Availability:

Code	Name	Occurrence
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CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	3
FS	File Segment	2
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
BSO	Beilstein Citation	1
DED	Entry Date	1
DUPD	Update Date	1
CRYPH	Crystal Phase	1
MP	Melting Point	2

This substance also occurs in Reaction Documents:

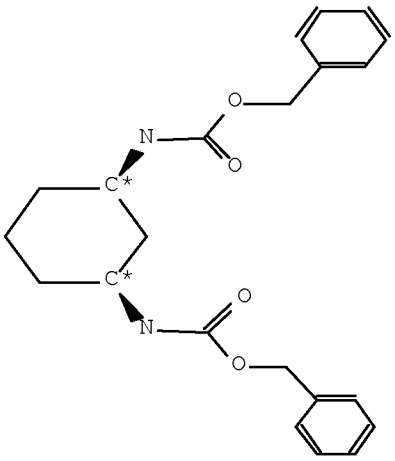
Code	Name	Occurrence
RX	Reaction Documents	2
RXREA	Substance is Reaction Reactant	1
RXPRO	Substance is Reaction Product	1

All References:
ALLREF

1. Hewgill; Jefferies, J.Chem.Soc., CODEN: JCSOA9, <1956>, 805,807

L79 ANSWER 14 OF 38 BEILSTEIN COPYRIGHT 2008 BEILSTEIN MDL on STN

Beilstein Records (BRN):	3223184
Chemical Name (CN):	N,N'-(cis-cyclohexane-1,3-diyl)-bis-carbamic acid dibenzyl ester
Autonom Name (AUN):	(3-benzyloxycarbonylamino-cyclohexyl)-carbamic acid benzyl ester
Molec. Formula (MF):	C22 H26 N2 O4
Molecular Weight (MW):	382.46
Lawson Number (LN):	14460, 5228, 1762
File Segment (FS):	Stereo compound
Compound Type (CTYPE):	isocyclic
Constitution ID (CONSID):	2951475
Tautomer ID (TAUTID):	3156779
Beilstein Citation (BSO):	4-13-00-00011
Entry Date (DED):	1990/02/15
Update Date (DUPD):	1990/02/15



Field Availability:

Code	Name	Occurrence
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	3
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
BSO	Beilstein Citation	1
DED	Entry Date	1
DUPD	Update Date	1
MP	Melting Point	1

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	2
RXREA	Substance is Reaction Reactant	1
RXPRO	Substance is Reaction Product	1

All References:
ALLREF

1. Hewgill; Jefferies, J.Chem.Soc., CODEN: JCSOA9, <1956>, 805,807

L79 ANSWER 15 OF 38 USPATFULL on STN
ACCESSION NUMBER: 2007:211271 USPATFULL Full-text
TITLE: Therapeutic agents I
INVENTOR(S): Evertsson, Emma, Molndal, SWEDEN

Inghardt, Tord, Molndal, SWEDEN
Lindberg, Jan, Molndal, SWEDEN
Linusson, Anna, Umea, SWEDEN
Giordanetto, Fabrizio, Molndal, SWEDEN
PATENT ASSIGNEE(S): ASTRAZENECA AB, Sodertalje, SWEDEN (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2007185079	A1	20070809	
APPLICATION INFO.:	US 2005-596994	A1	20050105	(10)
	WO 2005-SE4		20050105	
			20061122	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	GB 2004-25209	20041116
	GB 2004-196	20040107

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Pepper Hamilton LLP, 500 Grant Street, One Mellon Bank Center, 50th Floor, Pittsburgh, PA, 15219-2502, US
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1
LINE COUNT: 3962

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds of formula(I), processes for preparing such compounds, their use in the treatment of obesity, psychiatric disorders, cognitive disorders, memory disorders, schizophrenia, epilepsy, and related conditions, and neurological disorders such as dementia, multiple sclerosis, Parkinson's disease, Huntington's chorea and Alzheimer's disease and pain related disorders, and pharmaceutical compositions containing them. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD (1S,3S)-Cyclohexane-1,3-diamine dihydrochloride

DETD 2-chloroquinoline-4-carbonyl chloride (4.4 g, 19.5 mmol) was added to an ice-cold solution of dimethyl amine hydrochloride (1.6 g, 19.5 mmol) in Et.sub.3N (5.4 mL) and DCM (46 mL). The ice bath was removed and the reaction. . .

CLM What is claimed is:

19. A compound selected from one or more of: (1S,3S)-Dibenzyl-cyclohexane-1,3-diylbiscarbamate; and (1S,3S)-Cyclohexane-1,3-diamine dihydrochloride.

IT 92-15-9P 1578-96-7P 2388-32-1P 4002-83-9P 5652-13-1P
6188-43-8P, Imidazo[1,2-a]pyridine-3-carboxaldehyde 6953-22-6P
10102-94-0P 13523-92-7P 20507-53-3P 25233-47-0P 27257-15-4P
30198-01-7P 40053-37-0P 52173-35-0P 58630-07-2P 67509-84-6P
67999-51-3P 83783-33-9P 89445-80-7P 97892-67-6P 106792-38-5P
131237-81-5P 156496-64-9P 171919-36-1P 238756-47-3P 238756-48-4P
271241-24-8P 271241-25-9P 276862-85-2P 406204-74-8P 441715-30-6P
444683-23-2P 482585-36-4P 645400-43-7P 645400-44-8P 645400-49-3P
645400-50-6P 860296-82-8P 860296-85-1P 860296-97-5P
860297-00-3P 860297-02-5P 860297-04-7P 860297-06-9P 860297-08-1P
860297-09-2P 860297-11-6P 860297-12-7P 860297-13-8P 860297-14-9P
860297-15-0P 860297-16-1P 860297-17-2P 860297-18-3P 860297-19-4P
860297-20-7P 860297-21-8P 860297-22-9P 860297-23-0P 860297-24-1P
860297-25-2P 860297-26-3P 860297-27-4P 860297-28-5P 860297-29-6P
860297-30-9P 860297-31-0P 860297-32-1P 860297-33-2P 860297-34-3P

860297-35-4P 860297-36-5P 860297-37-6P 860297-38-7P 860297-39-8P
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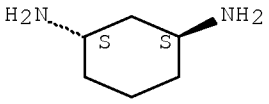
860297-45-6P 860297-46-7P 860297-47-8P 860297-48-9P 860297-49-0P
860297-50-3P 860297-51-4P 860434-14-6P
(preparation of quinoline derivs. as MCH modulators)
IT 860296-82-8P
(preparation of quinoline derivs. as MCH modulators)
RN 860296-82-8 USPATFULL
CN 1,3-Cyclohexanediamine, dihydrochloride, (1S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

L79 ANSWER 16 OF 38 USPATFULL on STN
ACCESSION NUMBER: 2006:118393 USPATFULL Full-text
TITLE: Chemokine receptor binding heterocyclic compounds with enhanced efficacy
INVENTOR(S): Bridger, Gary, Bellingham, WA, UNITED STATES
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	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2006100240	A1	20060511
APPLICATION INFO.:	US 2005-301725	A1	20051213 (11)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2003-457034, filed on 6 Jun 2003, PENDING Continuation-in-part of Ser. No. US 2003-446170, filed on 23 May 2003, PENDING Continuation-in-part of Ser. No. US 2002-329329, filed on 23 Dec 2002, ABANDONED

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2001-342716P	20011221 (60)	<--
	US 2002-350822P	20020117 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MORRISON & FOERSTER LLP, 12531 HIGH BLUFF DRIVE, SUITE

100, SAN DIEGO, CA, 92130-2040, US
NUMBER OF CLAIMS: 38
EXEMPLARY CLAIM: 1
LINE COUNT: 13517
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to heterocyclic compounds consisting of a core nitrogen atom surrounded by three pendant groups, wherein two of the three pendant groups are preferably benzimidazolyl methyl and tetrahydroquinolyl, and the third pendant group contains N and optionally contains additional rings. The compounds bind to chemokine receptors, including CXCR4 and CCR5, and demonstrate protective effects against infection of target cells by a human immunodeficiency virus (HIV).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . pH, the compounds of the invention will be in the forms of the acid addition salts. Particularly preferred are the hydrochlorides. In addition, when prepared as purified forms, the compounds may also be crystallized as the hydrates.
DETD To a stirred solution of (2-aminomethyl)benzimidazole dihydrochloride hydrate (5.96 g, 27.1 mmol) in dry MeOH (225 mL) was added 6,7-dihydro-5H-quinolin-8-one (3.99 g, 27.1 mmol) and the mixture. . .
DETD COMPOUND 18: Preparation of N'-(1H-benzimidazol-2-ylmethyl)-N'-(5)-5,6,7,8-tetrahydro-quinolin-8-yl-butane-1,4-diamine (hydrochloride salt)
DETD . . . General Procedure B: To a stirred solution of 4-[(1H-Benzoimidazole-2-ylmethyl)-(5,6,7,8-tetrahydro-quinolin-8-yl)-amino]-butyraldehyde (see COMPOUND 32 for preparation) (0.2182 g, 0.63 mmol) and aminoguanadine hydrochloride (69 mg, 0.63 mmol) in dry MeOH (4 mL) was added AcOH (75 μL, 1.26 mmol) and the mixture was. . .
DETD A solution of N.sup.1-(5,6,7,8-tetrahydro-quinolin-8-yl)-N.sup.1-[1-(2-trimethylsilanyl-ethoxymethyl)-1H-benzoimidazol-2-ylmethyl]-butane-1,4-diamine (170 mg, 0.35 mmol), 1-H-pyrazole-1-carboxamidine hydrochloride (51 mg, 0.35 mmol) and DIPEA (61 μL, 0.35 mmol) in THF (0.2 mL) was stirred at room temperature for. . .
DETD To a stirred solution of 4-(methylamino)-butyric acid hydrochloride (303 mg, 1.97 mmol) and dioxane (2 mL) in saturated aqueous NaHCO.sub.3 (2 mL) was added added di-tert-butyl di-carbonate (523. . .
DETD COMPOUND 44: Preparation of (trans-2-aminomethyl-cyclopropylmethyl)-(1H-benzimidazol-2-ylmethyl)-(S)-5,6,7,8-tetrahydroquinlin-8-yl-amine (hydrochloride salt)
DETD Preparation of (trans-2-aminomethyl-cyclopropylmethyl)-(1H-benz-imidazol-2-ylmethyl)-(S)-5,6,7,8-tetrahydroquinlin-8-yl-amine (hydrochloride salt) (COMPOUND 44)
DETD To a solution of the crude aldehyde from above (90 mg, 0.17 mmol) in methanol (1.5 mL) was added hydroxyamine hydrochloride salt (23 mg, 0.33 mmol) and the mixture was stirred at room temperature for 40 minutes. The mixture was concentrated. . .
DETD A solution of trans-4-aminocyclohexanol hydrochloride (2.67 g, 1.14 mol) in 1 N NaOH (40 mL) was washed with CHCl.sub.3 (40 mL), CH.sub.2Cl.sub.2 (2×30 mL) and. . .
DETD COMPOUND 55: Preparation of N.sup.1-(1H-Benzimidazol-2-ylmethyl)-N.sup.1-((S)-5,6,7,8-tetrahydro-quinolin-8-yl)-trans-cyclohexane-1,4-diamine (hydrochloride salt)
DETD To a solution of trans-4-aminocyclohexanol hydrochloride (10.0 g, 65.9 mmol) and triethylamine (18.4 mL, 132.0 mmol) in tetrahydrofuran (132 mL) was added di-tert-butyl dicarbonate (15.31 g,. . .
DETD To a stirred suspension of (Z)-4-chloro-2-butenylamine hydrochloride (1.0 g, 7.0 mmol) in THF (35 mL) and water (0.2 mL) was added N,N-diisopropylethylamine (2.7 mL, 15.4 mmol) followed. . .

DETD COMPOUND 76: Preparation of (Z)-N.sup.1-(1H-Benzimidazol-2-ylmethyl)-N.sup.1-5,6,7,8-tetrahydro-quinolin-8-yl-but-2-ene-1,4-diamine (hydrochloride salt)

DETD (Z)-4-chloro-2-butenylamine hydrochloride (3.88 g, 27.3 mmol), water (1 mL) and diisopropylethylamine (9.6 mL, 55.1 mmol) were dissolved in tetrahydrofuran (140 mL) and. . .

DETD To a stirred mixture of 1-amino-4-chloro-2-butyne hydrochloride (1.12 g, 8.01 mmol) and Boc.sub.2O (2.12 g, 9.71 mmol) in a solution of THF (40 mL) and H.sub.2O (15. . .

DETD A solution of trans-2-aminocyclohexanol hydrochloride (1.185 g, 7.81 mmol) and 2-nitrobenzenesulfonyl chloride (1.73 g, 7.81 mmol) in CH.sub.2Cl.sub.2 (20 mL) was cooled in an ice. . .

DETD . . . was then washed with diethyl ether (3×20 mL) and dried in vacuo. This afforded the required 4-[(1H-benzimidazol-2-ylmethyl)-(5,6,7,8-tetrahydroquinolin-8-yl)-amino]-butyrimidic acid methyl ester (hydrochloride salt), which was used immediately in the next reaction.

DETD To a solution of (1-H-benzimidazol-2-ylmethyl)-(5,6,7,8-tetrahydro-quinolin-8-yl)-(1-(N-phthalimidyl)-butan-2-one-4-yl)-amine (58 mg, 0.117 mmol) in methanol (5 mL) was added hydroxylamine hydrochloride (83.5 mg, 1.0 mmol). The resulting solution was stirred at room temperature overnight. Aqueous sodium bicarbonate (5 mL of a. . .

DETD . . . mmol). The resulting suspension was stirred for 10 minutes, then a solution of 3-nitroanisole (1.55 g, 10.1 mmol) and methoxylamine hydrochloride (1.08 g, 12.9 mmol) in DMF (15 mL) was added in a dropwise manner over 15 minutes. The mixture was. . .

DETD COMPOUND 102: Preparation of N.sup.1-(1-Methyl-1H-benzoimidazol-2-ylmethyl)-N.sup.1-(S)-(5,6,7,8-tetrahydro-quinolin-8-yl)-butane-1,4-diamine hydrochloride salt

DETD COMPOUND 107: Preparation of N.sup.1-(1H-Benzimidazol-2-ylmethyl)-N.sup.1-(S)-3,4-dihydro-2H-pyrano[3,2-b]pyridin-4-yl-butane-1,4-diamine (hydrochloride salt)

DETD A solution of the ketone (2.9 g, 19 mmol) from above and hydroxylamine hydrochloride (1.6 g, 23 mmol) in methanol (100 mL) was stirred at room temperature for 1 h. Saturated sodium bicarbonate solution. . .

DETD Preparation of N.sup.1-(1H-Benzimidazol-2-ylmethyl)-N.sup.1-(S)-3,4-dihydo-2H-pyrano[3,2-b]pyridin-4-yl-butane-1,4-diamine hydrochloride salt (COMPOUND 107)

DETD Following General Procedure D: Conversion of the free base (1.80 g, 5.1 mmol) from above to the hydrochloride salt gave COMPOUND 107 (2.14 g, 82%) as a white solid. .sup.1H NMR (D.sub.2O) δ 1.49-1.60 (m, 4H), 2.39-2.49 (m,. . .

DETD COMPOUND 114: Preparation of N.sup.1-(4-Methoxy-1H-benzoindiazol-2-ylmethyl)-N.sup.1-(S)-(5,6,7,8-tetrahydro-quinolin-8-yl)-butane-1,4-diamine)hydrochloride salt)

DETD COMPOUND 123: Preparation of N.sup.1-(1-Allyl-1H-benzimidazol-2-ylmethyl)-N.sup.1-(S)-5,6,7,8-tetrahydro-quinolin-8-yl-butane-1,4-diamine (hydrochloride salt)

DETD To a solution of 4-(hydroxymethyl)imidazole hydrochloride (578 mg, 4.30 mmol) in DMF (3.5 mL) was added DIPEA (1.9 mL, 10.9 mmol) and 2-(trimethylsilyl)ethoxymethyl chloride (0.83 mL,. . .

DETD COMPOUND 135: Preparation of N.sup.1-(1-Allyl-1H-imidazol-2-ylmethyl)-N.sup.1-(S)-5,6,7,8-tetrahydro-quinolin-8-yl-butane-1,4-diamine (Hydrochloride salt)

DETD Following general procedure D, conversion of the material to his hydrochloride salt and re-precipitation from methanol/diethylether gave COMPOUND 135 (7.97 g, 82%) as beige solid. .sup.1H NMR (300 MHz, D.sub.2O, δ. . .

DETD . . . the above amine (173 mg, 0.52 mmol) in DMF (3 mL) was added 1-hydroxybenzotriazole hydrate (104 mg, 0.77 mmol), 1-(3-

dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (148 mg, 0.77 mmol), and 6-hydroxynicotinic acid (86 mg, 0.62 mmol). The reaction was stirred overnight at room temperature. Then. . .

DETD . . . solution of N.sup.1-(1H-benzoimidazol-2-ylmethyl)-N.sup.1-(5,6,7,8-tetrahydro-quinolin-8-yl)-propane-1,3-diamine (166 mg, 0.50 mmol) in DMF (3 mL) was added 1-hydroxybenzotriazole hydrate (100 mg, 0.74 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (142 mg, 0.74 mmol), and benzoic acid (73 mg, 0.59 mmol). The reaction mixture was stirred overnight at room temperature.. . .

DETD . . . of 5-bromonicotinic acid (120 mg, 0.60 mmol) in DMF (3 mL) was added 1-hydroxybenzotriazole hydrate (96 mg, 0.72 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (137 mg, 0.72 mmol), N,N-diisopropylethylamine (0.21 mL, 1.19 mmol), and N.sup.1-(1H-benzoimidazol-2-ylmethyl)-N.sup.1-(5,6,7,8-tetrahydro-quinolin-8-yl)-propane-1,3-diamine (200 mg, 0.60 mmol). The reaction mixture was stirred. . .

DETD . . . of cinnoline-4-carboxylic acid (80 mg, 0.46 mmol) in DMF (3 mL) was added 1-hydroxybenzotriazole hydrate (74 mg, 0.55 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (106 mg, 0.55 mmol), N,N-diisopropylethylamine (0.16 mL, 0.92 mmol), and N.sup.1-(1H-benzoimidazol-2-ylmethyl)-N.sup.1-(5,6,7,8-tetrahydro-quinolin-8-yl)-propane-1,3-diamine (154 mg, 0.46 mmol). The reaction mixture was stirred. . .

DETD 4-[(1-Allyl-1H-benzoimidazol-2-ylmethyl)-(5,6,7,8-tetrahydro-quinolin-8-yl)-amino]-butyl hydrochloride salt (120 mg, 0.215 mmol) was neutralized with 1M NaOH (25 mL) and the free base was extracted with CHCl.sub.3. . .

DETD N.sup.1-(1-Allyl-1H-imidazol-2-ylmethyl)-N.sup.1-(S)-5,6,7,8-tetrahydro-quinolin-8-yl-butane-1,4-diamine, Hydrochloride salt (115.1 mg, 0.216 mmol) was neutralized with 1M NaOH (25 mL) and the free base was extracted with CHCl.sub.3. . .

DETD COMPOUND 157: Preparation of (Cis-2-Aminomethyl-cylcopropylmethyl)-(1H-benzimidazol-2-ylmethyl)-(S)-5,6,7,8-tetrahydro-quinolin-8-yl-amine (hydrochloride salt)

DETD Preparation of (Cis-2-Aminomethyl-cylcopropylmethyl)-(1H-benzimidazol-2-ylmethyl)-(S)-5,6,7,8-tetrahydro-quinolin-8-yl-amine (hydrochloride salt) (COMPOUND 157)

DETD Following General Procedure D: Conversion of the free base (2.80 g, 7.7 mmol) from above to the hydrochloride salt provided COMPOUND 157 (3.30 g, 87%) as a white solid. 1H NMR (D.sub.2O) δ 0.08 (q, 1H, J=5.0 Hz),. . .

DETD ((1R,2S)-2-Aminomethyl-cylcopropylmethyl)-(1H-benzimidazol-2-ylmethyl)-(S)-5,6,7,8-tetrahydro-quinolin-8-yl-amine, hydrochloride salt (107.2 mg, 0.217 mmol) was neutralized with 1M NaOH (25 mL) and the free base was extracted with CHCl.sub.3. . .

DETD 3-Aminomethyl-N-(1H-benzoimidazol-2-ylmethyl)-N-(5,6,7,8-tetrahydro-quinolin-8-yl)-but-2-ene-1,4-diamine, hydrochloride salt (213.8 mg, 0.365 mmol) was neutralized with 1M NaOH (25 mL) and the free base was extracted with CHCl.sub.3. . .

DETD COMPOUND 160: 3-Aminomethyl-N.sup.1-(1H-benzoimidazol-2-ylmethyl)-N.sup.1-(S)-(5,6,7,8-tetrahydro-quinolin-8-yl)-but-2-ene-1,4-diamine hydrochloride salt

DETD Preparation of carbonic acid pyrrolidin-3-ylmethyl ester vinyl ester hydrochloride

DETD . . . was added THF (4 mL), Et.sub.3N (0.58 mL, 4.2 mmol), and a solution of carbonic acid pyrrolidin-3-ylmethyl ester vinyl ester hydrochloride (284 mg, 1.37 mmol) in THF (3 mL), and the mixture was stirred at room temperature for 21 h. The. . .

IT 65-85-0, Benzoic acid, reactions 75-31-0, Isopropylamine, reactions

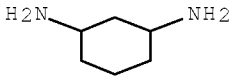
79-33-4, L-Lactic acid, reactions 93-10-7, Quinoline-2-carboxylic acid 93-53-8, 2-Phenylpropionaldehyde 93-97-0, Benzoic anhydride 95-54-5, 1,2-Phenylenediamine, reactions 96-32-2, Methyl bromoacetate 98-97-5, 2-Pyrazinecarboxylic acid 98-98-6, Picolinic acid 100-46-9, Benzylamine, reactions 100-52-7, Benzaldehyde, reactions 100-58-3, Phenylmagnesium bromide 104-98-3, Urocanic acid 105-36-2, Ethyl bromoacetate 106-95-6, Allyl bromide, reactions 107-11-9, Allylamine 107-18-6, Allyl alcohol, reactions 110-63-4, 1,4-Butanediol, reactions 110-91-8, Morpholine, reactions 123-72-8, Butyraldehyde 124-02-7, Diallylamine 156-87-6, 3-Amino-1-propanol 273-21-2, 4-Azabenzimidazole 288-32-4, Imidazole, reactions 487-89-8, Indole-3-carboxaldehyde 504-02-9, 1,3-Cyclohexanedione 555-03-3, 3-Nitroanisole 592-57-4, 1,3-Cyclohexadiene 603-35-0, Triphenylphosphine, reactions 609-65-4, 2-Chlorobenzoyl chloride 616-29-5, 1,3-Diamino-2-hydroxypropane 616-30-8, 3-Amino-1,2-propanediol 617-52-7, Dimethyl itaconate 623-27-8, 1,4-Benzenedicarboxaldehyde 627-27-0, 3-Buten-1-ol 765-30-0, Cyclopropylamine 822-36-6, 4-Methylimidazole 826-34-6, Dimethyl cis-1,2-cyclopropanedicarboxylate 867-13-0, Triethyl phosphonoacetate 1074-82-4, Potassium phthalimide 1099-45-2, (Carbethoxymethylene)triphenylphosphorane 1121-60-4, Pyridine-2-carboxaldehyde 1126-09-6, Ethyl isonipecotate 1477-50-5, Indole-2-carboxylic acid 1694-92-4, 2-Nitrobenzenesulfonyl chloride 2605-67-6, Methyl (triphenylphosphoranylidene)acetate 2615-25-0, trans-1,4-Cyclohexanediamine 2859-68-9, 3-(2-Pyridyl)-1-propanol 3012-80-4, 1-Methyl-1H-benzimidazole-2-carboxaldehyde 3385-21-5 , 1,3-Cyclohexanediamine 3433-37-2, 2-Piperidinemethanol 3752-24-7, 4,5,6,7-Tetrahydro-1H-benzimidazole 3920-50-1, Pyrazole-3-carboxaldehyde 3999-55-1, Diethyl trans-1,2-cyclopropanedicarboxylate 4023-02-3, 1H-Pyrazole-1-carboxamidine hydrochloride 4048-33-3, 6-Amino-1-hexanol 4606-65-9, 3-Piperidinemethanol 4760-34-3, N-Methyl-o-phenylenediamine 4856-97-7, 2-Hydroxymethylbenzimidazole 5006-66-6, 6-Hydroxynicotinic acid 5130-24-5, Vinyl chloroformate 5332-06-9, 4-Bromobutyronitrile 5332-24-1, 3-Bromoquinoline 5382-16-1, 4-Hydroxypiperidine 5414-21-1, 5-Bromovaleronitrile 5456-63-3, trans-2-Aminocyclohexanol hydrochloride 5731-17-9, (1-Benzylpyrrolidin-3-yl)methanol 5993-91-9, 2-(Aminomethyl)benzimidazole dihydrochloride 6602-32-0, 2-Bromo-3-pyridinol 6624-49-3, 3-Isoquinolinecarboxylic acid 6859-99-0, 3-Hydroxypiperidine 6976-17-6, 4-(Methylamino)butyric acid hydrochloride 7051-34-5, (Bromomethyl)cyclopropane 7153-66-4, (Z)-4-Chloro-2-butenylamine hydrochloride 7197-96-8, 2,3-Cycloheptenopyridine 10111-08-7, Imidazole-2-carboxaldehyde 13325-10-5, 4-Amino-1-butanol 13750-81-7, 1-Methyl-2-imidazolecarboxaldehyde 13958-93-5, 3,5-Dichloroisonicotinic acid 14080-23-0, 2-Cyanopyrimidine 14631-46-0, 8-Hydroxy-5,6,7,8-tetrahydroquinoline 16139-18-7, Aminoguanidine hydrochloride 20826-04-4, 5-Bromonicotinic acid 21905-86-2, Cinnoline-4-carboxylic acid 22059-21-8, 1-Aminocyclopropanecarboxylic acid 26690-80-2, (2-Hydroxyethyl)carbamic acid tert-butyl ester 29602-39-9, 2-[(2-Aminoethyl)amino]-5-nitropyridine 31106-82-8, 2-(Bromomethyl)pyridine hydrobromide 32673-41-9, 4-(Hydroxymethyl)imidazole hydrochloride 33036-62-3, 4-Bromobutan-1-ol 34413-35-9, 5,6,7,8-Tetrahydroquinoxaline 38666-30-7, 5,6,7,8-Tetrahydroimidazo[1,5-a]pyridine 42383-61-9, 2-Aminoimidazole sulfate 46153-01-9, 2-Methyl-5,6-dihydro-4H-imidazo[4,5,1-ij]quinoline 50910-54-8, trans-4-Aminocyclohexanol hydrochloride 53054-03-8, (2S)-5-Amino-2-(tert-butoxycarbonylamino)pentanoic acid tert-butyl ester 58885-58-8, (3-Hydroxypropyl)carbamic acid tert-butyl ester 61388-89-4, 2-Methyl-8-acetamidoquinoline 66715-65-9, 2-Pyridinesulfonyl chloride

68076-36-8, (4-Aminobutyl)carbamic acid tert-butyl ester 69610-41-9, N-(tert-Butoxycarbonyl)-L-prolinal 72998-92-6, 2-Chloromethyl-5,6-dimethyl-1H-benzimidazole 76513-69-4, [2-(Trimethylsilyl)ethoxy]methyl chloride 77369-59-6, 1-Amino-4-chloro-2-butyne hydrochloride 80567-69-7, 2-Chloromethyl-4-methyl-1H-benzimidazole 102089-74-7, (R)-N-(tert-Butoxycarbonyl)-2-phenylglycinol 104249-15-2, N-((E)-4-Bromo-2-butenyl)phthalimide 107430-29-5, 2-Chloromethyl-6-trifluoromethyl-1H-benzimidazole 117049-14-6, (S)-N-(tert-Butoxycarbonyl)-2-phenylglycinol 125163-05-5, 8-Hydroxy-4-methoxy-5,6,7,8-tetrahydroquinoline 130861-73-3, 2-Chloro-8-hydroxy-5,6,7,8-tetrahydroquinoline 156144-42-2, 2-Chloromethyl-5-fluoro-1H-benzimidazole 157634-00-9, 2-Hydroxymethylpiperidine-1-carboxylic acid tert-butyl ester 163798-87-6, 1-(tert-Butoxycarbonyl)-2-chloromethylbenzimidazole 229328-97-6, 3,5-Dichloroisonicotinoyl chloride 298181-83-6, 8-Amino-5,6,7,8-tetrahydroquinoline 369655-84-5, ((R)-5,6,7,8-Tetrahydroquinolin-8-yl)amine 369656-57-5, (S)-5,6,7,8-Tetrahydroquinolin-8-ylamine 405173-68-4, 2-Chloromethyl-4,5-dimethyl-1H-benzimidazole 405173-94-6, 2-Chloromethyl-7-fluoro-1H-benzimidazole 405174-39-2, 4-(4-Fluorophenyl)-1-[(2-trimethylsilanylethoxy)methyl]-1H-imidazole-2-carboxaldehyde 507228-47-9, [tert-Butoxycarbonylimino(4-oxopiperidin-1-yl)methyl]carbamic acid tert-butyl ester 558441-93-3, 4-[(1H-Benzimidazole-2-ylmethyl)(5,6,7,8-tetrahydroquinolin-8-yl)amino]butyraldehyde 558442-56-1, [[1-(tert-Butoxycarbonyl)benzimidazol-2-yl]methyl](5,6,7,8-tetrahydroquinolin-8-yl)[(4S)-4-phenyl-4-(tert-butoxycarbonylamino)butyl]amine 558442-84-5, N1-(1H-Benzimidazol-2-ylmethyl)-N1-(5,6,7,8-tetrahydroquinolin-8-yl)-N4-benzylcyclohexane-trans-1,4-diamine 558443-56-4, [[1-(tert-Butoxycarbonyl)-1H-benzimidazol-2-yl]methyl](5,6,7,8-tetrahydroquinolin-8-yl)(3-cyanopropyl)amine 558443-80-4, 2-[4-(tert-Butyldimethylsilanyloxy)-2-hydroxybutyl]isoindole-1,3-dione 558444-72-7, 2-[4-[((S)-5,6,7,8-Tetrahydroquinolin-8-yl)amino]butyl]isoindole-1,3-dione 558445-48-0, 2-Chloromethyl-4-methoxybenzimidazole-1-carboxylic acid tert-butyl ester 558446-25-6, N-(5,6,7,8-Tetrahydroquinolin-8-yl)butane-1,4-diamine 558447-10-2, N'-((S)-5,6,7,8-Tetrahydroquinolin-8-yl)butane-1,4-diamine 558447-26-0, N'-(1H-Benzimidazol-2-ylmethyl)-N'-((S)-5,6,7,8-tetrahydroquinolin-8-yl)butane-1,4-diamine 558447-80-6, 4-[[(1-Allyl-1H-benzimidazol-2-yl)methyl]((S)-5,6,7,8-tetrahydroquinolin-8-yl)amino]butylamine hydrochloride 558447-89-5, (1H-Benzimidazol-2-ylmethyl)((S)-5,6,7,8-tetrahydroquinolin-8-yl)amine 558447-98-6, 3-Aminomethyl-N-(1H-benzimidazol-2-ylmethyl)-N-(5,6,7,8-tetrahydroquinolin-8-yl)but-2-ene-1,4-diamine hydrochloride
(preparation of chemokine receptor binding benzimidazolylmethyl tetrahydroquinolinyl amines and related heterocyclic compds. with enhanced efficacy against AIDS and other disorders)

IT 3385-21-5, 1,3-Cyclohexanediamine
(preparation of chemokine receptor binding benzimidazolylmethyl tetrahydroquinolinyl amines and related heterocyclic compds. with enhanced efficacy against AIDS and other disorders)

RN 3385-21-5 USPATFULL

CN 1,3-Cyclohexanediamine (CA INDEX NAME)



L79 ANSWER 17 OF 38 USPATFULL on STN
ACCESSION NUMBER: 2006:211066 USPATFULL Full-text
TITLE: Purine derivatives and processes for their preparation
INVENTOR(S): Zimmermann, Jurg, Wallbach, SWITZERLAND
Capraro, Hans-Georg, Rheinfelden, SWITZERLAND
Imbach, Patricia, Riehen, SWITZERLAND
Furet, Pascal, Thann, FRANCE
PATENT ASSIGNEE(S): Novartis AG, Basel, SWITZERLAND (non-U.S. corporation)

	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 7091346	B1	20060815		
	WO 9716452		19970509		<--
APPLICATION INFO.:	US 1996-51827		19961022	(9)	<--
	WO 1996-EP4573		19961022		<--
			19980501	PCT 371 date	

	NUMBER	DATE	
PRIORITY INFORMATION:	CH 1995-3094	19951101	<--
	CH 1996-2213	19960910	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Berch, Mark L.
LEGAL REPRESENTATIVE: McNally, Lydia T.
NUMBER OF CLAIMS: 1
EXEMPLARY CLAIM: 1
LINE COUNT: 3092
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB 2-Amino-6-anilino-purine derivatives of the formula 1

##STR1## in which the symbols are as defined in claim 1 are described.

These compounds inhibit p34.sup.cdc2/cyclin B.sup.cdc13 kinase and can be used for treatment of hyperproliferative diseases, for example tumour diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AI 19961022
19980501 PCT 371 date
SUMM . . . catalysts, condensation agents (for example phosphorus pentoxide) or neutralizing agents, for example bases, in particular nitrogen bases, such as triethylamine hydrochloride, depending on the nature of the reaction and/or of the reaction participants, at a reduced, normal or elevated temperature, for. . .
DETD . . . 6-(3-chloro-phenyl-amino)-9-ethyl-2-(3-formylamino-piperidin-1-yl)-9H-purine is obtained from 308 mg (1.0 mmol) of 2-chloro-6-(3-chloro-phenyl-amino)-9-ethyl-9H-purine [described in Stage 1.2], 190 mg (1.1 mmol of 3-amino-piperidine dihydrochloride and 0.314 ml (2.1 mmol) of 1,8-diazabicyclo[5.4.0]undec-7-ene(1.5-5)(=DBU) in 7.5 ml of dimethylformamide in a glass pressure reactor after 40 h. . .
DETD . . . 2-[(S)-1-carbamoyl-ethylamino]-6-(3-chloro-phenyl-amino)-9-ethyl-9H-purine is obtained from 308 mg (1.0 mmol) of 2-chloro-6-(3-chloro-phenyl-amino)-9-ethyl-9H-purine [described in Stage 1.2], 137 mg (1.1 mmol) of L-alaninamide hydrochloride [i.e.

(S)-(+)-2-amino-propionamide] and 0.314 ml (2.1 mmol) of 1,8-diazabicyclo[5.4.0]undec-7-ene(1.5-5)(=DBU) in 3.0 ml of dimethyl sulfoxide in a glass pressure reactor. . .

DETD Analogously to Example 1, 2-(2-amino-2-methyl-propyl-amino)-6-(3-chloro-phenyl-amino)-9-ethyl-9H-purine hydrochloride is obtained from 462 mg (1.5 mmol) of 2-chloro-6-(3-chloro-phenyl-amino)-9-ethyl-9H-purine [described in Stage 1.2] and 4.45 ml of 1,2-diamino-2-methyl-propane after 8. . .

DETD . . . 2-[3-amino-pyrrolidin-1-yl]-6-(3-chloro-phenyl-amino)-9-ethyl-9H-purine is obtained from 462 mg (1.5 mmol) of 2-chloro-6-(3-chloro-phenyl-amino)-9-ethyl-9H-purine [described in Stage 1.2], 262 mg (1.65 mmol) of 3-amino-pyrrolidine dihydrochloride and 0.417 ml (2.1 mmol) of 1,8-diazabicyclo[5.4.0]undec-7-ene(1.5-5)(=DBU) in 3.0 ml of dimethyl sulfoxide in a glass pressure reactor after 24. . .

DETD . . . 2-[carbamoyl-methyl-amino]-6-(3-chloro-phenyl-amino)-9-ethyl-9H-purine is obtained from 462 mg (1.5 mmol) of 2-chloro-6-(3-chloro-phenyl-amino)-9-ethyl-9H-purine [described in Stage 1.2], 121.6 mg (1.1 mmol of glycinamide hydrochloride and 0.314 ml (2.1 mmol) of 1,8-diazabicyclo[5.4.0]undec-7-ene(1.5-5)(=DBU) in 3.0 ml of dimethyl sulfoxide in a glass pressure reactor after 18. . .

DETD . . . 6-(3-chloro-phenyl-amino)-9-ethyl-2-(trans-4-hydroxy-cyclohexyl-amino)-9H-purine is obtained from 616 mg (2.00 mmol) of 2-chloro-6-(3-chloro-phenyl-amino)-9-ethyl-9H-purine [described in Stage 1.2], 607 mg (4.0 mmol) of trans-4-amino-cyclohexanol hydrochloride and 1.315 ml (8.8 mmol) of 1,8-diazabicyclo-[5.4.0]undec-7-ene(1.5-5)(=DBU) after 3 days at 100° C., 3 days at 50° C. and purification. . .

DETD . . . 6-(3-chloro-phenylamino)-9-ethyl-[4-hydroxymethyl-(imidazolyl)]-9H-purine is obtained from 308 mg (1.0 mmol) of 2-chloro-6-(3-chloro-phenyl-amino)-9-ethyl-9H-purine [described in Stage 1.2], 148 mg (1.1 mmol) of 4-(hydroxymethyl)-imidazole hydrochloride and 0.314 ml (2.1 mmol) of DBU in 2.5 ml of dimethyl sulfoxide in a glass pressure reactor after 48. . .

DETD . . . 6-(3-chloro-phenyl-amino)-2-(trans-2-hydroxy-cyclohexylamino)-9-ethyl-9H-purine is obtained from 308 mg (1.0 mmol) of 2-chloro-6-(3-chloro-phenyl-amino)-9-ethyl-9H-purine [described in Stage 1.2], 166.8 mg (1.1 mmol) of trans-2-amino-cyclohexanol hydrochloride and 0.314 ml (2.1 mmol) of DBU in 2 ml of dimethylsulfoxide after 24 h at 130° C. and purification. . .

DETD . . . a solid oil from 308 mg (1.0 mmol) of 2-chloro-6-(3-chloro-phenyl-amino)-9-ethyl-9H-purine [described in Stage 1.2], 177 mg (1.1 mmol) of cis-2-amino-cyclohexanol hydrochloride and 0.314 ml (2.1 mmol) of DBU in 2.0 ml of dimethyl sulfoxide in a glass pressure reactor after 17. . .

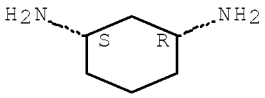
DETD . . . After removal of the solvent, the residue is dissolved in dioxane, and treated with 4 N HCl in dioxane. 2-(2-Amino-ethyl-amino)-9-ethyl-6-(3-fluor-phenyl-amino)-9H-purine hydrochloride is obtained as a crystalline precipitate by this procedure. This precipitate is filtered off and dried; m.p.>250° C.; FAB-MS: (M+H).sup.+=315;. . .

DETD . . . the solvent, the residue is dissolved in 3 ml of dioxane and treated with 4 N HCl in dioxane. 2-(2-Amino-ethyl-amino)-6-(3-cyano-phenyl-amino)-9-ethyl-9H-purine hydrochloride is obtained as a crystalline precipitate. This is filtered off and dried; m.p. 200° C.; FAB-MS: (M+H).sup.+=323; R.sub.f=0.5 (ethyl acetate:i-propanol:water:. . .

DETD Analogously to Example 90, 2-(2-amino-ethyl-amino)-6-(4-fluoro-phenyl-amino)-9-isopropyl-9H-purine hydrochloride is obtained from 0.2 g (0.52 mmol) of 2-chloro-9-isopropyl-6-(4-fluoro-phenyl-amino)-9H-purine

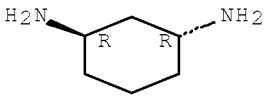
in 2.5 ml of ethylenediamine after 48 h at 75° C.;. . .
DETD Analogously to Example 91, 2-(2-amino-ethyl-amino)-9-ethyl-6-(4-fluoro-phenyl-amino)-9H-purine hydrochloride is obtained in crystalline form from 0.24 g (0.68 mmol) of 2-chloro-9-ethyl-6-(4-fluoro-phenyl-amino)-9H-purine in 2.5 ml of ethylenediamine after 48 h. . .
DETD . . . is dissolved in dioxane. The crystalline precipitate obtained after dropwise addition of 4 N HCl in dioxane, which is 2-hydrazino-6-(3-methoxy-phenyl-amino)-9-isopropyl-9H-purine hydrochloride, is filtered off and dried; m.p. 250° C.; FAB-MS: (M+H).sup.+=314; R.sub.f=0.5 (CH.sub.2Cl.sub.2:methanol=95:5).
DETD Analogously to Example 91, 2-(2-amino-ethyl-amino)-9-ethyl-6-(3-nitro-phenyl-amino)-9H-purine hydrochloride is obtained as a crystalline compound from 0.22 g (0.7 mmol) of 2-chloro-9-isopropyl-6-(4-nitro-phenyl-amino)-9H-purine in 3 ml of ethylenediamine after 2. . .
IT 51-85-4, Cystamine 61-54-1, Tryptamine 64-04-0, Phenethylamine 78-90-0, 1,2-Diaminopropane 95-54-5, 1,2-Phenylenediamine, reactions 98-16-8, 3-(Trifluoromethyl)aniline 100-01-6, reactions 100-46-9, Benzylamine, reactions 107-15-3, 1,2-Ethanediamine, reactions 108-42-9, 3-Chloroaniline 108-45-2, 1,3-Benzenediamine, reactions 108-49-6, 2,6-Dimethylpiperazine 108-91-8, Cyclohexylamine, reactions 109-76-2, 1,3-Propanediamine 109-81-9, N-Methylethylenediamine 110-85-0, Piperazine, reactions 111-40-0 111-42-2, Diethanolamine, reactions 124-68-5 140-31-8, 1-Piperazineethanamine 156-87-6, 3-Amino-1-propanol 177-11-7, 1,4-Dioxa-8-azaspiro[4.5]decane 288-32-4, Imidazole, reactions 371-40-4, 4-Fluoroaniline 372-19-0, 3-Fluoroaniline 505-19-1, Hexahydropyridazine 534-03-2, 2-Amino-1,3-propanediol 536-90-3, m-Anisidine 617-89-0, 2-Furfurylamine 622-58-2, p-Tolyl isocyanate 624-83-9, Methyl isocyanate 768-94-5, 1-Aminoadamantane 811-93-8, 1,2-Diamino-2-methylpropane 1001-53-2, N-Acetylethylenediamine 1119-28-4, 3-Aminopropionitrile fumarate 1121-22-8, trans-1,2-Diaminocyclohexane 1436-59-5, cis-1,2-Diaminocyclohexane 1477-55-0, 1,3-Bis(aminomethyl)benzene 1609-86-5, tert-Butyl isocyanate 1668-10-6, Glycinamide hydrochloride 2038-03-1, 4-(2-Aminoethyl)morpholine 2237-30-1, 3-Aminobenzonitrile 2615-25-0, trans-1,4-Diaminocyclohexane 2706-56-1, 2-(2-Aminoethyl)pyridine 2799-16-8 2799-17-9, S-(+)-1-Amino-2-propanol 2842-38-8, 2-(Cyclohexylamino)ethanol 3173-53-3, Cyclohexyl isocyanate 4000-72-0, 1-(Aminomethyl)-1-cyclohexanol 4403-69-4, 2-Aminobenzylamine 4795-29-3, Tetrahydrofurfurylamine 5332-73-0, 3-Methoxypropylamine 5382-16-1, 4-Hydroxypiperidine 5451-40-1, 2,6-Dichloropurine 5456-63-3, trans-2-Aminocyclohexanol hydrochloride 5856-62-2, S-(+)-2-Amino-1-butanol 5856-63-3 6321-23-9, 4-Methylcyclohexylamine 6936-47-6, cis-2-Aminocyclohexanol hydrochloride 7324-05-2 7531-52-4, L-Prolinamide 10316-79-7 15827-56-2, cis-1,4-Diaminocyclohexane 15932-66-8, 2-(2-Aminoethyl)piperidine 20439-47-8, (1R,2R)-(-)-1,2-Diaminocyclohexane 21436-03-3 23356-96-9, L-Prolinol 26772-34-9, cis-1,3-Diaminocyclohexane 26883-70-5, trans-1,3-Diaminocyclohexane 27578-60-5, 1-Piperidineethanamine 30651-60-6, 1-Aminopiperazine 32673-41-9, 4-(Hydroxymethyl)imidazole hydrochloride 50910-54-8, trans-4-Aminocyclohexanol hydrochloride 57414-85-4, Ethyl 3-amino-2-methylbenzoate 62937-45-5 68832-13-3, D-Prolinol 103831-11-4, 3-Aminopyrrolidine dihydrochloride 190655-14-2
(preparation of antitumor purine derivs.)
IT 26772-34-9, cis-1,3-Diaminocyclohexane 26883-70-5, trans-1,3-Diaminocyclohexane
(preparation of antitumor purine derivs.)
RN 26772-34-9 USPATFULL
CN 1,3-Cyclohexanediamine, (1R,3S)-rel- (CA INDEX NAME)

Relative stereochemistry.



RN 26883-70-5 USPATFULL
CN 1,3-Cyclohexanediamine, (1R,3R)-rel- (CA INDEX NAME)

Relative stereochemistry.



L79 ANSWER 18 OF 38 USPATFULL on STN
ACCESSION NUMBER: 2006:146745 USPATFULL Full-text
TITLE: Quinazolinones
INVENTOR(S): Mederski, Werner, Zwingenberg, GERMANY, FEDERAL REPUBLIC OF
Devant, Ralf, Darmstadt, GERMANY, FEDERAL REPUBLIC OF
Barnickel, Gerhard, Darmstadt, GERMANY, FEDERAL REPUBLIC OF
Bernotat-Danielowski, Sabine, Bad Nauheim, GERMANY, FEDERAL REPUBLIC OF
Melzer, Guido, Hofheim/Taunus, GERMANY, FEDERAL REPUBLIC OF
Cezanne, Bertram, Morfelden-Walldorf, GERMANY, FEDERAL REPUBLIC OF
Dhanoa, Daljit, Del Mar, CA, UNITED STATES
Zhao, Bao-Ping, West Windsor, NJ, UNITED STATES
Rinker, James, Kenhorst, PA, UNITED STATES
Player, Mark, Phoenixville, PA, UNITED STATES
Soll, Richard, Lawrencehill, NJ, UNITED STATES
PATENT ASSIGNEE(S): 3-Dimensional Pharmaceuticals, Inc., Exton, PA, UNITED STATES (U.S. corporation)

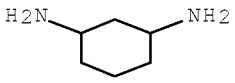
	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 7060706	B1	20060613		
	WO 2001023364		20010405		<--
APPLICATION INFO.:	US 2000-89167		20000913	(10)	<--
	WO 2000-EP8939		20000913		<--
			20020829	PCT 371 date	

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1999-325777P	19990928 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Balasubramanian, Venkataraman

LEGAL REPRESENTATIVE: Woodcock Washburn LLP
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 1264
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Quinazolinones of formula (I) in which R, R.sup.1, R.sup.2, R.sup.3, R.sup.4, Y, n and m have the meaning indicated in Patent claim 1, and their salts or solvates as glycoprotein IbIX antagonists ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AI 20000913
20020829 PCT 371 date
SUMM . . . carried out in an inert solvent as indicated above in the presence of a dehydrating agent, such as, dicyclohexylcarbodiimide (DCC), N-(3-dimethylaminopropyl)-N'-ethyl-carbodiimide-hydrochlorid (EDC) or diisopropylcarbodiimide (DIC), further for instance in the presence of an anhydride of propanphosphonic acid (see Angew. Chem. 1980,. . .
IT 66-77-3, Naphthalene-1-carbaldehyde 66-99-9, Naphthalene-2-carbaldehyde 98-03-3, Thiophene-2-carbaldehyde 100-52-7, Benzaldehyde, reactions 104-53-0, 3-Phenylpropionaldehyde 104-55-2, 3-Phenylpropenal 104-87-0, 4-Methylbenzaldehyde 118-92-3, Anthranilic acid 123-11-5, 4-Methoxybenzaldehyde, reactions 498-62-4, Thiophene-3-carbaldehyde 529-20-4, 2-Methylbenzaldehyde 587-04-2, 3-Chlorobenzaldehyde 591-31-1, 3-Methoxybenzaldehyde 620-23-5, 3-Methylbenzaldehyde 939-97-9, 4-tert-Butylbenzaldehyde 2043-61-0, Cyclohexanecarbaldehyde 2549-93-1, [[4-(Aminomethyl)cyclohexyl]methyl]amine 2579-20-6, [[3-(Aminomethyl)cyclohexyl]methyl]amine 3114-70-3, Cyclohexane-1,4-diamine 3218-36-8, Biphenyl-4-carbaldehyde 3385-21-5, Cyclohexane-1,3-diamine 3779-27-9, [2,2']Bithiophenyl-5-carbaldehyde 4543-51-5, 3-Furan-2-ylpropenal 6203-18-5, 3-(4-Dimethylaminophenyl)propenal 10035-16-2, Benzofuran-5-carbaldehyde 13234-45-2, 2-[4-(2-Aminoethyl)cyclohexyl]ethylamine 13338-82-4, 4-(Aminomethyl)cyclohexylamine 40027-36-9, 2-[3-(2-Aminoethyl)cyclohexyl]ethylamine 97087-59-7, 3-(Aminomethyl)cyclohexylamine 129288-64-8, 3-(3-Aminopropyl)cyclohexylamine 150256-42-1, N-Fmoc-anthranilic acid 202256-86-8, 4-(2-Aminoethyl)cyclohexylamine 332121-81-0, 3-(2-Aminoethyl)cyclohexylamine 332121-82-1, [[3-(2-Aminoethyl)cyclohexyl]methyl]amine 332121-83-2, [[3-(3-Aminopropyl)cyclohexyl]methyl]amine 332121-84-3, 3-[3-(3-Aminopropyl)cyclohexyl]propylamine 332121-85-4, 4-(3-Aminopropyl)cyclohexylamine 332121-86-5, [[4-(2-Aminoethyl)cyclohexyl]methyl]amine 332121-87-6, [[4-(3-Aminopropyl)cyclohexyl]methyl]amine 332121-88-7, 3-[4-(3-Aminopropyl)cyclohexyl]propylamine 332121-90-1, N-Fmoc-5-chloroanthranilic acid 332121-91-2, N-Fmoc-5-methylanthranilic acid 332121-92-3, N-Fmoc-4-chloroanthranilic acid 332121-93-4, N-Fmoc-5-methoxyanthranilic acid
(precursor; preparation of quinazolinone derivs. as glycoprotein IbIX antagonists)
IT 3385-21-5, Cyclohexane-1,3-diamine
(precursor; preparation of quinazolinone derivs. as glycoprotein IbIX antagonists)
RN 3385-21-5 USPATFULL
CN 1,3-Cyclohexanediamine (CA INDEX NAME)



L79 ANSWER 19 OF 38 USPATFULL on STN
ACCESSION NUMBER: 2005:131933 USPATFULL Full-text
TITLE: Imidazo[1,2-a]pyridine derivative
INVENTOR(S): Takemura, Makoto, Edogawa-ku, JAPAN
Takahashi, Hisashi, Edogawa-ku, JAPAN
Kawakami, Katsuhiro, Edogawa-ku, JAPAN
Takeshita, Hiroshi, Edogawa-ku, JAPAN
Kimura, Youichi, Edogawa-ku, JAPAN
Watanabe, Jun, Edogawa-ku, JAPAN
Sugimoto, Yuichi, Edogawa-ku, JAPAN
Kitamura, Akihiro, Edogawa-ku, JAPAN
Nakajima, Ryohei, Edogawa-ku, JAPAN
Kanai, Kazuo, Edogawa-kun, JAPAN
Fujisawa, Tetsunori, Takaoka-shi, JAPAN

	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 2005113397	A1	20050526		
APPLICATION INFO.:	US 2003-502971	A1	20030130	(10)	<--
	WO 2003-JP912		20030130		<--

	NUMBER	DATE	
PRIORITY INFORMATION:	JP 2002-22767	20020131	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: SUGHRUE MION, PLLC, 2100 PENNSYLVANIA AVENUE, N.W., SUITE 800, WASHINGTON, DC, 20037, US
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
LINE COUNT: 9053
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A compound reprsented by the following formula (I), its salts or nsolvates thereof capable of specifically or selectively expressig an antifungal activity in a broad spectrum based on the novel mechanism thereof of 1,6-β-glucan synthesis inhibition, and an antifungal agent containing any of them. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AI 20030130
SUMM . . . used for external applications for therapy of superficial mycosis, including, for example, various azole-type medicines, and polyenemacrolide-type nystatin, griseofulvin, terbinafine hydrochloride, butenafine hydrochloride and amorolfine chloride. On the other hand, for therapy of deep-seated mycosis that is significantly on the increase these days,. . .
SUMM Examples of the acid addition salt include inorganic acid salts such as hydrochlorides, sulfates, nitrate, hydrobromides, hydroiodides and phosphates; and organic acid salts such as methanesulfonates,

benzenesulfonates, para-toluenesulfonates (sulfonates), acetates, citrates, maleates, fumarates,. . .

DETD To N,N-dimethylformamide (2.5 ml) suspension of 163 mg (0.50 mmol) of 1-chloro-2-n-hexyl-3-methylpyrido[1,2-a]benzimidazole-4-carbonitrile were added 95.2 mg (0.55 mmol) of 3-dimethylaminoazetidine dihydrochloride and 349 μl (2.50 mol) of triethylamine, and the resultng mixture was heated at 80° C. for 10 hours. After. . .

DETD To N,N-dimethylformamide (5.0 ml) suspension of 326 mg (1.00 mmol) of 1-chloro-2-n-hexyl-3-methylpyrido[1,2-a]benzimidazole-4-carbonitrile were added 191 mg (1.02 mmol) of 3-(dimethylaminomethyl)azetidine dihydrochloride and 0.56 ml (4.00 mmol) of triethylamine, and the resulting mixture was heated at 80° C. for 15 hours. After. . .

DETD 2-n-Hexyl-3-methyl-1-[3-dimethylaminomethylpyrroldin-1-yl]pyrido[1,2-a]benzimidazole-4-carbonitrile dihydrochloride

DETD . . . pyrrolidin1-yl

40	(3S)-N'-methylaminopyrrolidine	[(3S)-N'-methylamino]-pyrrolidin-1-yl	334
41	(3R)-N'-ethylaminopyrrolidine	[(3R)-N'-ethylamino]-pyrrolidin-1-yl	347
42	(3R)-N',N'-dimethylaminopyrrolidine	[(3R)-N',N'-dimethylamino]-pyrrolidin-1-yl	347
43	(±)-3-aminopiperidine dihydrochloride	(3-aminopiperidin)-1-yl	334
44	(±)-3-aminopiperidine dihydrochloride	(3-piperidinyl)amino	334
45	4-N',N'-dimethylaminopiperidine	(4-N',N'-dimethylamino)-piperidin-1-yl	362
46	(±)-3-N'-methylaminopiperidine dihydrochloride	(3-N'-methylamino)-piperidin-1-yl	320
47	4-pyrrolidinopiperidine	(4-pyrrolidinopiperidin)-1-yl	388

DETD 2-(3-Aminopropyl)-1-[(3S)-dimethylaminopyrrolidin-1-yl)-3-methylpyrido[1,2-a]benzimidazole-4-carbonitrile trihydrochloride (I-47)

DETD 287 μl (2.06 mol) of triethylamine was added to dichloromethane (5 ml) suspension of 200 mg (412 μmol) of 2-(3-aminopropyl)-1-[(3S)-dimethylaminopyrrolidin-1-yl]-3-methylpyrido[1,2-a]benzimidazole-4-carbonitrile trihydrochloride (I-47) and 58 μl (617 μmol) of acetic anhydride at 0° C., and the resulting mixture was stirred at room. . .

DETD 287 μl (2.06 mol) of triethylamine was added to dichloromethane (4 ml) suspension of 200 mg (412 μmol) of 2-(3-aminopropyl)-1-[(3S)-dimethylaminopyrrolidin-1-yl]-3-methylpyrido[1,2-a]benzimidazole-4-carbonitrile trihydrochloride (I-47) and 142 μl (617 μmol) of di-tert-butyl dicarbonate at 0° C., and the resulting mixture was stirred at room. . .

DETD 2-(3-Aminopropyl)-1-[(3S)-dimethylaminopyrrolidin-1-yl]-3-methylpyrido[1,2-a]benzimidazole-4-carbonitrile trihydrochloride (#77)

DETD . . . (15.8 mmol) of ethyl 3,4-diaminobenzoate were added 1.48 g (17.4 mmol) of cyanoacetic acid, 3.64 g (19.0 mmol) of 1-ethyl-3-(3-diethylaminopropyl)carbodiimide hydrochloride and 2.14 g (15.8 mmol) of 1-hydroxybenzotriazole, and the resulting mixture was stirred at room temperature for 15 hours. The. . .

DETD Ethyl 2-n-butyl-4-cyano-1-(2-N', N'-diethylaminoethylamino)-3-methylpyrido[1,2-a]benzimidazole-8-carboxylate (#97) and ethyl 2-n-butyl-4-cyano-1-(2-N', N'-diethylaminoethylamino)-3-methylpyrido[1,2-a]benzimidazole-7-carboxylate hydrochloride (#98)

DETD . . . under reduced pressure, and the residue was recrystallized

from methanol/ethanol to obtain 232 mg (24%) of the entitled compound (7-ester hydrochloride, #98) as ayellow crystal. 8-ethyl ester (#97)

DETD 7-ethyl ester hydrochloride (#98)

DETD . . . from 2.65 g (15.0 mmol) of 4,5-dichloro-1,2-phenylenediamine, 1.40 g (16.5 mmol) of cyanoacetic acid, 3.45 g (18.0 mmol) of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride and 2.03 g (15.0 mmol) of 1-hydroxybenzotriazole. (Not crystallized, this was directly used in the next reaction.)

DETD . . . from 3.52 g (25.9 mmol) of 4,5-dimethyl-1,2-phenylenediamine, 2.42 g (28.5 mmol) of cyanoacetic acid, 5.95 g (31.0 mmol) of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride and 3.49 g (25.9 mmol) of 1-hydroxybenzotriazole.

DETD Ethyl [(3S)-pyrrolidin-3-yl]methylaminoacetate dihydrochloride (I-96)

DETD To N,N-dimethylformamide (15 ml) suspension of 714 mg (2.75 mmol) of ethyl [(3S)-pyrrolidin-3-yl]methylaminoacetate dihydrochloride (I-96) were added 2.16 ml (15.5 mmol) of triethylamine and 492 mg (1.55 mmol) of 1-chloro-3-methyl-2-phenylpyrido[1,2-a]benzimidazole-4-carbonitrile (I-8). The system was. . .

DETD (3S)-3-[[2-(tert-Butoxycarbonylamino)ethyl]methylamino]-pyrrolidine dihydrochloride (I-98)

DETD According to the production method for (#103), N,N-dimethylformamide (9 ml) solution of 336 mg (1.06 mmol) of (3S)-3-[[2-(tert-butoxycarbonylamino)ethyl]methylamino]-pyrrolidine dihydrochloride (I-98), 617 μl (4.43 mmol) of triethylamine and 281 mg (885 μmol) of 1-chloro-3-methyl-2-phenylpyrido[1,2-a]benzimidazole-4-carbonitrile (I-8) was heated at 80° C.. . .

DETD (3S)-3-[(2-Hydroxyethyl)methylamino]pyrrolidine dihydrochloride (I-101)

DETD According to the production method for (#103), N,N-dimethylformamide (10 ml) solution of 221 mg (972 μmol) of (3S)-3-[(2-hydroxyethyl)methylamino]pyrrolidine dihydrochloride (I-101), 677 μl (4.86 mmol) of triethylamine and 309 mg (972 μmol) of 1-chloro-3-methyl-2-phenylpyrido[1,2-a]benzimidazole-4-carbonitrile (I-8) was heated at 80° C.. . .

DETD . . . (556 μmol) of 1-chloro-2-ethyl-3-methylpyrido[1,2-a]benzimidazole-4-carbonitrile (I-2) were added 249 μl (1.67 mmol) of 1,8-diazabicyclo[5.4.0]-7-undecene and 113 mg (667 μmol) of 2-diethylaminoethanethiol hydrochloride. The system was replaced with nitrogen and sealed up, and stirred at room temperature for 2.5 hours. The solvent was. . .

DETD . . . compound was dissolved in dichloromethane (8 ml) and 435 μl (3.12 mmol) of triethylamine, 99 mg (1.01 mmol) of N,O-dimethylhydroxylamine hydrochloride, 137 mg (1.01 mmol) of 1-hydroxybenzotriazole and 99 mg (1.01 mmol) of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride were added thereto in nitrogen atmosphere at room temperature. At the temperature, this was stirred for 12 hours, and aqueous. . .

DETD . . . was suspended in dimethylsulfoxide (4 ml), and 0.37 ml (2.64 mmol) of triethylamine and 142 mg (0.82 mmol) of N,N-dimethyl-3-azetidinamine dihydrochloride were added thereto, and heated with stirring at 90° C. for 18 hours. After restored to room temperature, water was. . .

DETD . . . mmol) of ethyl 2,3-diaminobenzoate (I-171) were added 561 mg (6.60 mmol) of cyanoacetic acid, 1.38 g (7.20 mmol) of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride and 810 mg (6.00 mmol) of 1-hydroxybenzotriazole, and then the resulting mixture was stirred at room temperature for 4 hours.. . .

DETD With cooling with ice, 6.26 g (32.6 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride was added to dichloromethane solution of 3.32 g (27.2 mmol) of 3-methylbenzene-1,2-diamine (I-176),

2.78 g (27.2 mmol) of cyanoacetic acid. . .

DETD . . . mmol) of methanol and 0.15 g (1.2 mmol) of 4-(dimethylamino)pyridine. After cooling with ice, 26.8 g (140 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride was added thereto, and the resulting mixture was stirred overnight with gradually warming up to room temperature. The reaction mixture. . .

DETD . . . ml) solution of 5.0 g (29.0 mmol) of (3,5-difluorophenyl)acetic acid. After cooling with ice, 6.68 g (34.9 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride was added thereto, and stirred for 22 hours with gradually warming up to room temperature. The reaction mixture was concentrated. . .

DETD . . . added 84 μl (0.6 mmol) of triethylamine, 27 mg (0.2 mmol) of 1-hydroxybenzotriazole hydrate, 41 mg (0.5 mmol) of dimethylamine hydrochloride and 58 mg (0.3 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, and the resulting mixture was stirred overnight at room temperature. The reaction mixture was concentrated under reduced pressure, and the. . .

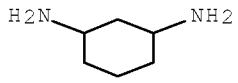
IT 50-00-0, Formaldehyde, reactions 62-55-5, Thioacetamide 64-17-5, Ethanol, reactions 67-56-1, Methanol, reactions 75-36-5, Acetyl chloride 79-20-9, Methyl acetate 85-41-6, Phthalimide 93-89-0, Ethyl benzoate 96-09-3, Styrene oxide 96-35-5, Methyl glycolate 98-88-4, Benzoyl chloride 100-11-8, 4-Nitrobenzyl bromide 100-36-7, 2-(Diethylamino)ethylamine 100-39-0, Benzyl bromide 100-46-9, Benzylamine, reactions 100-52-7, Benzaldehyde, reactions 105-45-3, Methyl acetoacetate 105-54-4, Ethyl butyrate 105-56-6, Ethyl cyanoacetate 106-31-0, Butyric anhydride 106-88-7, 1,2-Butylene oxide 107-30-2, Chloromethyl methyl ether 108-00-9, N,N-Dimethylethylenediamine 108-24-7, Acetic anhydride 109-01-3, N-Methylpiperazine 109-65-9, 1-Bromobutane 110-85-0, Piperazine, reactions 110-91-8, Morpholine, reactions 112-29-8, 1-Bromodecane 121-91-5, Isophthalic acid, reactions 123-75-1, Pyrrolidine, reactions 123-90-0, Thiomorpholine 124-40-3, Dimethylamine, reactions 124-63-0, Methanesulfonyl chloride 141-78-6, Ethyl acetate, reactions 141-97-9, Ethyl acetoacetate 142-25-6, N,N',N'-Trimethylethylenediamine 331-25-9, (3-Fluorophenyl)acetic acid 332-77-4, 2,5-Dimethoxy-2,5-dihydrofuran 372-09-8, Cyanoacetic acid 452-58-4, 2,3-Diaminopyridine 456-41-7, 3-Fluorobenzyl bromide 459-46-1, 4-Fluorobenzyl bromide 512-56-1, Trimethyl phosphate 517-23-7, 2-Acetylbutyrolactone 533-58-4, 2-Iodophenol 557-21-1, Zinc cyanide 570-24-1, 2-Methyl-6-nitroaniline 607-97-6, Ethyl 2-ethylacetoacetate 616-24-0, 1-Ethylpropylamine 620-79-1, Ethyl 2-benzylacetoacetate 626-27-7, Heptanoic anhydride 631-58-3, Thiopropionamide 638-07-3, Ethyl 4-chloroacetoacetate 696-59-3 813-19-4, Hexabutylditin 824-94-2, 4-Methoxybenzyl chloride 836-42-0, 4-Benzyloxybenzyl chloride 882-33-7, Diphenyl disulfide 1001-53-2, N-Acetylethylenediamine 1115-30-6, Diethyl 2-acetylsuccinate 1131-09-5, Benzo[b]thiophene-3-acetic acid 1521-51-3, 3-Bromocyclohexene 1522-41-4, Ethyl 2-fluoroacetoacetate 1522-46-9, Ethyl α-isopropylacetoacetate 1540-29-0, Ethyl 2-butylacetoacetate 1603-79-8, Ethyl phenylglyoxylate 1692-25-7, Pyridine-3-boronic acid 1759-53-1, Cyclopropanecarboxylic acid 1824-81-3, 2-Amino-6-picoline 1878-67-7, 3-Bromophenylacetic acid 1942-52-5, 2-Diethylaminoethanethiol hydrochloride 2038-03-1, 2-Morpholinoethylamine 2227-79-4, Thiobenzamide 2417-72-3, 4-Methoxycarbonylbenzyl bromide 3171-45-7, 4,5-Dimethyl-1,2-phenylenediamine 3218-02-8, Cyclohexanemethylamine 3249-68-1 3282-30-2, Pivaloyl chloride 3385-21-5, 1,3-Cyclohexanediamine 3958-57-4, 3-Nitrobenzyl bromide 4009-98-7, Methoxymethyltriphenylphosphonium chloride 4318-37-0, 1-Methylhomopiperazine 4414-88-4, (2-Benzimidazolyl)acetonitrile 4606-65-9, 3-Piperidinemethanol 5004-07-9, 4-Pyrrolidinopiperidine

5348-42-5, 4,5-Dichloro-1,2-phenylenediamine 5382-16-1, 4-Hydroxypiperidine 5396-89-4, Benzyl acetoacetate 5413-05-8, Ethyl 2-phenylacetoacetate 5437-45-6, Benzyl bromoacetate 5856-63-3, (R)-(-)-2-Amino-1-butanol 6079-97-6, Ethyl 2-hexylacetoacetate 6148-64-7, Malonic acid monoethyl ester potassium salt 6635-86-5, 2-Amino-4-methyl-3-nitropyridine 6638-79-5, N,O-Dimethylhydroxylamine hydrochloride 6921-34-2, Benzylmagnesium chloride 7152-15-0 7328-91-8 7677-24-9, Trimethylsilyl cyanide 7737-62-4, Ethyl 3-oxoheptanoate 14741-71-0, Ethyl (2-benzimidazolyl)acetate 17138-28-2, Ethyl (4-hydroxyphenyl)acetate 18107-18-1, Trimethylsilyl diazomethane 18927-05-4 22627-70-9, 3-Ethoxy-2-cyclopenten-1-one 23114-01-4, N-Methyl-N-nitro-p-toluenesulfonamide 23915-07-3, 2,4-Difluorobenzyl bromide 24424-99-5, Di-tert-butyl dicarbonate 27489-62-9, trans-4-Aminocyclohexanol 28611-39-4, 4-Dimethylaminophenylboronic acid 30414-53-0, Methyl 3-oxovalerate 37466-90-3, Ethyl 3,4-diaminobenzoate 39581-61-8 40499-83-0, 3-Pyrrolidinol 41051-15-4, Methyl 4-methoxy-3-oxobutyrate 50533-97-6, 4-Dimethylaminopiperidine 51207-66-0, (S)-(+)-1-(2-Pyrrolidinylmethyl)pyrrolidine 51644-96-3, 5-Aminopentylcarbamic acid tert-butyl ester 57260-73-8, 2-Aminoethylcarbamic acid tert-butyl ester 57382-97-5, Ethyl 2-thiopheneacetate 58479-61-1, tert-Butyldiphenylsilyl chloride 58859-46-4 62234-40-6 74879-18-8, (S)-2-Methylpiperazine 77326-45-5 79286-74-1, 3-(Acetylamino)pyrrolidine 89711-08-0 99724-17-1, 3-(Dimethylaminomethyl)pyrrolidine 102191-92-4, (tert-Butyldimethylsilyloxy)acetaldehyde 105184-38-1, (3,5-Difluorophenyl)acetic acid 119750-52-6 119750-56-0 124668-49-1 127199-45-5, (7S)-7-tert-Butoxycarbonylamino-5-azaspiro[2,4]heptane 127294-77-3, 3-Methylaminopiperidine dihydrochloride 128345-57-3, (3S)-Aminopyrrolidine 132883-44-4, (3S)-Dimethylaminopyrrolidine 132958-72-6, (3R)-Dimethylaminopyrrolidine 138060-07-8, 3-Aminopiperidine dihydrochloride 138619-76-8 139015-32-0 139015-33-1 169749-99-9 186203-81-6 192130-58-8 321890-22-6 381670-30-0 577776-81-9 577776-82-0 577776-97-7 577777-20-9
(preparation of imidazo[1,2-a]pyridine derivs. as antifungal agents with specific or selective 1,6-β-glucan)

IT 3385-21-5, 1,3-Cyclohexanediamine
(preparation of imidazo[1,2-a]pyridine derivs. as antifungal agents with specific or selective 1,6-β-glucan)

RN 3385-21-5 USPATFULL

CN 1,3-Cyclohexanediamine (CA INDEX NAME)



L79 ANSWER 20 OF 38 USPATFULL on STN

ACCESSION NUMBER: 2005:24074 USPATFULL Full-text

TITLE: 5-Substituted isoquinoline derivatives

INVENTOR(S): Yamada, Rintaro, Fuji-shi, JAPAN
Seto, Minoru, Fuji-shi, JAPAN

	NUMBER	KIND	DATE

PATENT INFORMATION: US 2005020623 A1 20050127
US 7094789 B2 20060822
APPLICATION INFO.: US 2003-623751 A1 20030722 (10) <--

	NUMBER	DATE
PRIORITY INFORMATION:	JP 2002-212053	20020722 <--
	JP 2002-327751	20021112 <--
	US 2002-397142P	20020722 (60) <--
	US 2002-425742P	20021113 (60) <--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BIRCH STEWART KOLASCH & BIRCH, PO BOX 747, FALLS CHURCH, VA, 22040-0747
NUMBER OF CLAIMS: 37
EXEMPLARY CLAIM: 1
LINE COUNT: 12306
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A compound represented by the following formula (1) or a salt thereof: ##STR1##

wherein R.sup.1 represents hydrogen atom, a halogen atom and the like; R.sup.2 represents hydrogen atom, a halogen atom, a C.sub.1-6 alkyl group and the like; and R.sup.3 represents --O--X--C(A.sup.1)(A.sup.11)--C(A.sup.2)(A.sup.21)--N(A.sup.31)(A.sup.3)(X represents propylene group etc., A.sup.11 and A.sup.21 represent hydrogen atom, or a C.sub.1-6 alkyl group, A.sup.31 represents a C.sub.1-6 alkyl group substituted with hydroxyl group, or hydrogen atom, and A.sup.1, A.sup.2, and A.sup.3 represent hydrogen atom, a C.sub.1-6 alkyl group and the like) and the like, which has an inhibitory activity on the phosphorylation of myosin regulatory light chain, and is useful for treatment of diseases relating to contraction of various cells and the like.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . J. Pharm. Sci., 66, 1-19 (1977). Examples of the acid addition salts include, for example, mineral acid salts such as hydrochlorides, hydrobromides, hydroiodides, nitrates, sulfates, and hydrogensulfates, phosphates, hydrogenphosphates, organic acid salts such as acetates, trifluoroacetates, gluconates, lactates, salicylates, citrates, tartrates,. . .
DETD . . . (e.g., timolol maleate and the like), selective β-adrenergic receptor antagonists (e.g., betaxolol and the like), cholinergic receptor agonists (e.g., pilocarpine hydrochloride and the like), choline esterase inhibitors (e.g., fisostigmine and the like), carbonic anhydrase inhibitors (e.g., brinzolamide and the like), prostaglandine derivatives (e.g., latanoprost and the like), non-selective sympatholytic agents (e.g., epinephrine hydrochloride and the like), selective α1 adrenergic receptor antagonists (e.g., bunazosin hydrochloride and the like), selective α2 adrenergic receptor antagonists (e.g., brimonidin tartrate and the like), α1- and β-adrenergic receptor antagonists (e.g., nipradilol and the like), α-adrenergic receptor agonists (e.g., dipivefrin hydrochloride and the like), calcium antagonists (e.g., iganidipin and the like), and so forth (AI Report, Cima Science Journal, 2002).
DETD . . . can be optionally chosen from suppressants of chemical mediator release (e.g., sodium cromoglicate and the like), anti-histamic agents (e.g., epinastine hydrochloride and the like), suppressants of lipid

mediator production, suppressants of Th2 cytokine production (e.g., suplatast tosilate and the like), bronchodilators,. . .

DETD [1055] N-[(5-Isoquinolyl)sulfonyl]-N-(3-phenylpropyl)-1,3-propylenediamine hydrochloride (Exemplary Compound No. 3-35)

DETD [1060] (Step C) Synthesis of N-[(5-isoquinolyl)sulfonyl]-N-(3-phenylpropyl)-1,3-propylenediamine hydrochloride

DETD [1064] N-[(5-Isoquinolyl)sulfonyl]-N-[2-(2-thienyl)ethyl-1,3-propylenediamine hydrochloride (Exemplary Compound No. 3-37)

DETD [1067] (Step B) Synthesis of N-[(5-isoquinolyl)sulfonyl]-N-[2-(2-thienyl)ethyl]-1,3-propylenediamine hydrochloride

DETD [1071] 4-{N-[(5-Isoquinolyl)sulfonyl]-N-(3-phenylpropyl)}aminopiperidine hydrochloride (Exemplary Compound No. 3-205)

DETD [1076] (Step C) Synthesis of 4-{N-[(5-isoquinolyl)sulfonyl]-N-(3-phenylpropyl)}-aminopiperidine hydrochloride

DETD [1080] N-[(5-Isoquinolyl)sulfonyl]-N-(4-phenylbutyl)-1,3-propylenediamine hydrochloride (Exemplary Compound No. 3-47)

DETD [1083] (Step B) Synthesis of N-[(5-isoquinolyl)sulfonyl]-N-(4-phenylbutyl)-1,3-propylenediamine hydrochloride

DETD [1087] N-[(4-Methyl-5-isoquinolyl)sulfonyl]-N-(3-phenylpropyl)-1,3-propylenediamine hydrochloride (Exemplary Compound No. 3-715)

DETD [1092] (Step C) Synthesis of N-[(4-methyl-5-isoquinolyl)sulfonyl]-N-(3-phenylpropyl)-1,3-propylenediamine hydrochloride

DETD [1096] N-[(5-Isoquinolyl)sulfonyl]-N-[2-(phenylsulfonyl)ethyl]-1,3-propylenediamine hydrochloride (Exemplary Compound No. 3-46)

DETD [1099] (Step B) Synthesis of N-[(5-isoquinolyl)sulfonyl]-N-[2-(phenylsulfonyl)ethyl]-1,3-propylenediamine hydrochloride

DETD [1103] N-[(5-Isoquinolyl)sulfonyl]-N-[2-(phenylsulfonyl)ethyl]ethylenediamine hydrochloride (Exemplary Compound No. 3-12)

DETD [1108] (Step C) Synthesis of N-[(5-isoquinolyl)sulfonyl]-N-[2-(phenylsulfonyl)ethyl]-ethylenediamine hydrochloride

DETD [1112] N-[(1-Amino-5-isoquinolyl)sulfonyl]-N-(3-phenylpropyl)-1,3-propylenediamine hydrochloride (Exemplary Compound No. 3-647)

DETD . . . (335 μl) in dichloromethane (3 ml) was added with a solution of (1-chloro-5-isoquinolyl)sulfonyl chloride (524 mg, prepared from (1-chloro-5-isoquinolyl)sulfonyl chloride hydrochloride according to the method of Japanese Patent Unexamined Publication (Kokai) No. 63-2980) in dichloromethane (3 ml) with stirring and ice. . .

DETD [1119] (Step D) Synthesis of N-[(1-amino-5-isoquinolyl)sulfonyl]-N-(3-phenylpropyl)-1,3-propylenediamine hydrochloride

DETD [1123] N-[(1-Amino-5-isoquinolyl)sulfonyl]-N-[2-(phenylsulfonyl)ethyl]ethylenediamine hydrochloride (Exemplary Compound No. 3-624)

DETD [1130] (Step D) Synthesis of N-[(1-amino-5-isoquinolyl)sulfonyl]-N-[2-(phenylsulfonyl)-ethyl]ethylenediamine hydrochloride

DETD [1134] 3-[(1-Amino-5-isoquinolyl)oxy]propylamine hydrochloride (Exemplary Compound No. 1-9)

DETD [1141] (Step D) Synthesis of 3-[(1-amino-5-isoquinolyl)oxy]propylamine hydrochloride

DETD [1145] 3-[(1 -Amino-5-isoquinolyl)oxy]methylpiperidine hydrochloride (Exemplary Compound No. 1-11)

DETD [1152] (Step D) Synthesis of 3-[(1-amino-5-isoquinolyl)oxy]methylpiperidine hydrochloride

DETD [1156] N-[(1-Hydroxy-5-isoquinolyl)sulfonyl]-N-[2-(phenylsulfonyl)ethyl]ethylenediamine hydrochloride (Exemplary Compound No. 3-318)

DETD [1159] (Step B) Synthesis of N-[(1-hydroxy-5-isoquinolyl)sulfonyl]-N-[2-(phenylsulfonyl)-ethyl]ethylenediamine hydrochloride

DETD [1163] N-[(1-Hydroxy-5-isoquinolyl)sulfonyl]-N-[2-(phenylsulfonyl)ethyl]-1,3-propylenediamine hydrochloride (Exemplary Compound No. 3-352)

DETD [1166] (Step B) Synthesis of N-[(1-hydroxy-5-isoquinolyl)sulfonyl]-N-[2-

(phenylsulfonyl)-ethyl]propylenediamine hydrochloride

DETD [1170] N-[(1-Hydroxy-5-isoquinolyl)sulfonyl]-N-(3-phenylpropyl)-1,3-propylenediamine hydrochloride (Exemplary Compound No. 3-341)

DETD [1173] (Step B) Synthesis of N-[(1-hydroxy-5-isoquinolyl)sulfonyl]-N-(3-phenylpropyl)-1,3-propylenediamine hydrochloride

DETD [1177] N-(5-Isoquinolyl)ethylenediamine hydrochloride

DETD [1180] (Step B) Synthesis of N-(5-isoquinolyl)ethylenediamine hydrochloride

DETD [1184] N-(5-Isoquinolyl)-1,3-propylenediamine hydrochloride (Exemplary Compound No. 2-1)

DETD [1187] (Step B) Synthesis of N-(5-isoquinolyl)-1,3-propylenediamine hydrochloride

DETD [1191] N-(5-Isoquinolyl)-N'-methyl-1,3-propylenediamine hydrochloride

DETD [1194] (Step B) Synthesis of N-(5-isoquinolyl)-N'-methyl-1,3-propylenediamine hydrochloride

DETD [1198] N-(5-Isoquinolyl)-1,4-butylenediamine hydrochloride (Exemplary Compound No. 2-2)

DETD [1201] (Step B) Synthesis of N-(5-isoquinolyl)-1,4-butylenediamine hydrochloride

DETD [1205] N-(5-Isoquinolyl)-pentamethylenediamine hydrochloride

DETD [1208] (Step B) Synthesis of N-(5-isoquinolyl)pentamethylenediamine hydrochloride

DETD [1212] 4-(5-Isoquinolyl)aminopiperidine hydrochloride (Exemplary Compound No. 2-4)

DETD [1215] (Step B) Synthesis of 4-(5-isoquinolyl)aminopiperidine hydrochloride

DETD [1219] 4-(5-Isbquinolyl)aminomethylpiperidine hydrochloride (Exemplary Compound No. 2-8)

DETD [1222] (Step B) Synthesis of 4-(5-isoquinolyl)aminomethylpiperidine hydrochloride

DETD [1226] 3-(5-Isoquinolyl)aminomethylpiperidine hydrochloride (Exemplary Compound No. 2-3)

DETD [1229] (Step B) Synthesis of 3-(5-isoquinolyl)aminomethylpiperidine hydrochloride

DETD [1233] Cis-N-(5-Isoquinolyl)-1,4-cyclohexanediamine hydrochloride (Exemplary Compound No. 2-5)

DETD [1244] (Step F) Synthesis of cis-N-(5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride

DETD [1248] Trans-N-(5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride (Exemplary Compound No. 2-6)

DETD [1253] (Step C) Synthesis of trans-N-(5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride

DETD [1257] N-(5-Isoquinolyl)-1,3-cyclohexanediamine hydrochloride (Exemplary Compound No. 2-7)

DETD [1262] (Step C) Synthesis of N-(5-isoquinolyl)-1,3-cyclohexanediamine hydrochloride

DETD [1266] N-(5-Isoquinolyl)-1,3-xylylenediamine hydrochloride (Exemplary Compound No. 2-11)

DETD [1269] (Step B) Synthesis of N-(5-isoquinolyl)-1,3-xylylenediamine hydrochloride

DETD [1273] 4-[(5-Isoquinolyl)oxy]piperidine hydrochloride (Exemplary Compound No. 1-2)

DETD [1276] (Step B) Synthesis of 4-[(5-isoquinolyl)oxy]piperidine hydrochloride

DETD [1280] 4-[N-(5-Isoquinolyl)-N-methyl]aminopiperidine hydrochloride (Exemplary Compound No. 2-114)

DETD [1282] A solution of methylamine hydrochloride (1.01 g, Wako Pure Chemical Industries) and 1-(tert-butoxycarbonyl)-4-oxopiperidine (1.99 g, Aldrich) in methanol (13 ml) was stirred in the presence. . .

DETD [1285] (Step C) 4-[N-(5-isoquinolyl)-N-methyl]aminopiperidine

hydrochloride
DETD [1288] 3-N-(5-Isoquinolyl)aminopiperidine hydrochloride (Exemplary Compound No. 2-10)
DETD [1291] (Step B) Synthesis of 3-N-(5-isoquinolyl)aminopiperidine hydrochloride
DETD [1302] 4-(4-Bromo-5-isoquinolylaminopiperidine hydrochloride (Exemplary Compound No. 2-181)
DETD [1305] (Step B) Synthesis of 4-(4-bromo-5-isoquinolyl)aminopiperidine hydrochloride
DETD [1309] 4-(4-Fluoro-5-isoquinolyl)aminopiperidine hydrochloride (Exemplary Compound No. 2-103)
DETD [1312] (Step B) Synthesis of 4-(4-fluoro-5-isoquinolyl)aminopiperidine hydrochloride
DETD [1316] 4-(4-Methylthio-5-isoquinolyl)aminopiperidine hydrochloride
DETD [1321] (Step C) Synthesis of 4-(4-methylthio-5-isoquinolyl)aminopiperidine hydrochloride
DETD [1325] 4-(4-Methyl-5-isoquinolyl)aminopiperidine hydrochloride (Exemplary Compound No. 2-70)
DETD [1328] (Step B) Synthesis of 4-(4-methyl-5-isoquinolyl)aminopiperidine hydrochloride
DETD [1332] N-(4-Bromo-5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride
DETD [1335] (Step B) Synthesis of N-(4-bromo-5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride
DETD [1338] N-(4-Fluoro-5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride
DETD [1341] (Step B) Synthesis of N-(4-fluoro-5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride
DETD [1344] N-(4-Methylthio-5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride
DETD [1347] (Step B) Synthesis of N-(4-methylthio-5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride
DETD [1350] 4-(4-Methanesulfinyl-5-isoquinolyl)aminopip eridine hydrochloride
DETD [1353] (Step B) Synthesis of 4-(4-methanesulfinyl-5-isoquinolyl)aminopiperidine hydrochloride
DETD [1357] 4-(4-Methanesulfonyl-5-isoquinolyl)aminopiperidine hydrochloride (Exemplary Compound No. 2-48)
DETD [1360] (Step B) Synthesis of 4-(4-methanesulfonyl-5-isoquinolyl)aminopiperidine hydrochloride
DETD [1363] 4-(4-Vinyl-5-isoquinolyl)aminopiperidine hydrochloride (Exemplary Compound No. 2-203)
DETD [1366] (Step B) Synthesis of 4-(4-vinyl-5-isoquinolyl)aminopiperidine hydrochloride
DETD [1370] 4-(4-Ethyl-5-isoquinolyl)aminopiperidine hydrochloride (Exemplary Compound No. 2-192)
DETD [1373] (Step B) Synthesis of 4-(4-ethyl-5-isoquinolyl)aminopiperidine hydrochloride
DETD [1386] 4-(1-Hydroxy-5-isoquinolyl)aminopiperidine hydrochloride (Exemplary Compound No. 2-59)
DETD [1390] N-(4-Vinyl-5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride
DETD [1393] (Step B) Synthesis of N-(4-vinyl-5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride
DETD [1396] N-(4-Ethyl-5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride
DETD [1399] (Step B) Synthesis of N-(4-ethyl-5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride
DETD [1402] 4-(4-Chloro-5-isoquinolyl)aminopiperidine hydrochloride
DETD [1413] (Step F) Synthesis of 4-(4-chloro-5-isoquinolyl)aminopiperidine hydrochloride
DETD [1417] N-(4-Chloro-5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride
DETD [1420] (Step B) Synthesis of N-(4-chloro-5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride
DETD [1423] Cis-N-(4-methyl-5-isoquinolyl)-1,4-cyclohexanediamine

hydrochloride (Exemplary Compound No. 2-71)

DETD [1428] (Step C) Synthesis of cis-N-(4-methyl-5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride

DETD [1432] Trans-N-(4-methyl-5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride (Exemplary Compound No. 2-72)

DETD [1435] (Step B) Synthesis of trans-N-(4-methyl-5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride

DETD [1439] 4-(4-Methoxy-5-isoquinolyl)aminopiperidine hydrochloride (Exemplary Compound No. 2-37)

DETD [1442] (Step B) Synthesis of 4-(4-methoxy-5-isoquinolyl)aminopiperidine hydrochloride

DETD [1446] N-(4-Methoxy-5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride

DETD [1449] (Step B) Synthesis of N-(4-methoxy-5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride

DETD [1452] N-[(5-Isoquinolyl)sulfonyl]-N-[3-(4-methanesulfonyl)phenylpropyl]-1,3-propylenediamine hydrochloride (Exemplary Compound No. 3-50)

DETD [1459] (Step D) Synthesis of N-[(5-isoquinolyl)sulfonyl]-N-[3-(4-methanesulfonyl)-phenylpropyl]-1,3-propylenediamine hydrochloride

DETD [1463] N-[(5-Isoquinolyl)sulfonyl]-N-[3-(3-methanesulfonyl)phenylpropyl]-1,3-propylenediamine hydrochloride (Exemplary Compound No. 3-49)

DETD [1472] (Step E) Synthesis of N-[(5-isoquinolyl)sulfonyl]-N-[3-(3-methanesulfonyl)-phenylpropyl]-1,3-propylenediamine hydrochloride

DETD [1475] N-[(5-Isoquinolyl)sulfonyl]-N-[3-(2-methanesulfonyl)phenylpropyl]-1,3-propylenediamine hydrochloride (Exemplary Compound No. 3-48)

DETD [1484] (Step E) Synthesis of N-[(5-isoquinolyl)sulfonyl]-N-[3-(2-methanesulfonyl)-phenylpropyl]-1,3-propylenediamine hydrochloride

DETD [1487] N-[(5-Isoquinolyl)sulfonyl]-N-[3-(4-carboxy)phenylpropyl]-1,3-propylenediamine hydrochloride

DETD [1494] (Step D) Synthesis of N-[(5-isoquinolyl)sulfonyl]-N-[3-(4-carboxy)phenylpropyl]-1,3-propylenediamine hydrochloride

DETD [1497] N-[(5-Isoquinolyl)sulfonyl]-N-[3-(3-carboxy)phenylpropyl]-1,3-propylenediamine hydrochloride

DETD [1504] (Step D) Synthesis of N-[(5-isoquinolyl)sulfonyl]-N-[3-(3-carboxy)phenylpropyl]-1,3-propylenediamine hydrochloride

DETD [1507] N-[(5-Isoquinolyl)sulfonyl]-N-[3-(2-carboxy)phenylpropyl]-1,3-propylenediamine hydrochloride

DETD [1514] (Step D) Synthesis of N-[(5-isoquinolyl)sulfonyl]-N-[3-(2-carboxy)phenylpropyl]-1,3-propylenediamine hydrochloride

DETD [1517] N-[(5-Isoquinolyl)sulfonyl]-N-[3-(4-methoxycarbonyl)phenylpropyl]-1,3-propylenediamine hydrochloride

DETD [1520] N-[(5-Isoquinolyl)sulfonyl]-N-[3-(3-methoxycarbonyl)phenylpropyl]-1,3-propylenediamine hydrochloride

DETD [1523] N-[(5-Isoquinolyl)sulfonyl]-N-[3-(2-methoxycarbonyl)phenylpropyl]-1,3-propylenediamine hydrochloride

DETD [1526] Trans-4-[(4-bromo-5-isoquinolyl)oxy]cyclohexylamine hydrochloride

DETD [1535] (Step E) Synthesis of trans-4-[(4-bromo-5-isoquinolyl)oxy]cyclohexylamine hydrochloride

DETD [1539] Trans-4-[(4-cyano-5-isoquinolyl)oxy]cyclohexylamine hydrochloride

DETD [1542] (Step B) Synthesis of trans-4-[(4-cyano-5-isoquinolyl)oxy]cyclohexylamine hydrochloride

DETD [1546] Trans-4-[(5-isoquinolyl)oxy]cyclohexylamine hydrochloride (Exemplary Compound No. 1-4)

DETD [1549] (Step B) Synthesis of trans-4-(5-isoquinolyloxy)cyclohexylamine hydrochloride

DETD [1553] Trans-4-[(4-vinyl-5-isoquinolyl)oxy]cyclohexylamine hydrochloride

DETD [1556] (Step B) Synthesis of trans-4-[(4-vinyl-5-isoquinolyl)oxy]cyclohexylamine hydrochloride

DETD [1560] Trans-4-[(4-amino-5-isoquinolyl)oxy]cyclohexylamine hydrochloride (Exemplary Compound No. 1-28)

DETD [1563] (Step B) Synthesis of trans-4-[(4-amino-5-

isoquinolyl)oxy]cyclohexylamine hydrochloride

DETD [1567] Trans-4-[(4-ethyl-5-isoquinolyl)oxy]cyclohexylamine hydrochloride

DETD [1570] (Step B) Synthesis of trans-4-[(4-ethyl-5-isoquinolyl)oxy]cyclohexylamine hydrochloride

DETD [1574] 4-[(4-Methyl-5-isoquinolyl)oxy]piperidine hydrochloride (Exemplary Compound No. 1-19)

DETD [1579] (Step C) Synthesis of 4-[(4-methyl-5-isoquinolyl)oxy]piperidine hydrochloride

DETD [1583] Trans-4-[(4-methyl-5-isoquinolyl)oxy]cyclohexylamine hydrochloride (Exemplary Compound No. 1-21)

DETD [1586] (Step B) Synthesis of trans-4-[(4-methyl-5-isoquinolyl)oxy]cyclohexylamine hydrochloride

DETD [1590] Cis-4-[(1-amino-5-isoquinolyl)oxy]cyclohexylamine hydrochloride (Exemplary Compound No. 1-13)

DETD [1595] (Step C) Synthesis of cis-4-[(1-amino-5-isoquinolyl)oxy]cyclohexylamine hydrochloride

DETD [1599] 4-(1-Amino-5-isoquinolyl)aminopiperidine hydrochloride (Exemplary Compound No. 2-12)

DETD [1608] 4-(4-Cyano-5-isoquinolyl)aminopiperidine hydrochloride

DETD [1613] (Step C) Synthesis of 4-(4-cyano-5-isoquinolyl)aminopiperidine hydrochloride

DETD [1617] 1-(2-Hydroxyethyl)-4-(5-isoquinolyl)aminopiperidine hydrochloride

DETD [1620] (Step B) Trans-1-[(4-cyano-5-isoquinolyl)oxy]-4-[(2-hydroxyethyl)amino]cyclohexane hydrochloride

DETD [1624] 1-(3-Hydroxypropyl)-4-(5-isoquinolyl)aminopiperidine hydrochloride

DETD [1627] 1-(2-Hydroxyethyl)-4-(4-methyl-5-isoquinolyl)aminopiperidine hydrochloride

DETD [1631] 1-(3-Hydroxypropyl)-4-(4-methyl-5-isoquinolyl)aminopiperidine hydrochloride

DETD [1634] Trans-N-(5-isoquinolyl)-N'-(2-hydroxyethyl)-1,4-cyclohexanediamine hydrochloride

DETD [1637] Trans-N-(5-isoquinolyl)-N'-(3-hydroxypropyl)-1,4-cyclohexanediamine hydrochloride

DETD [1640] Trans-N-(4-methyl-5-isoquinolyl)-N'-(2-hydroxyethyl)-1,4-cyclohexanediamine hydrochloride

DETD [1643] Trans-N-(4-methyl-5-isoquinolyl)-N'-(3-hydroxypropyl)-1,4-cyclohexanediamine hydrochloride

DETD [1646] Cis-N-(5-isoquinolyl)-N'-(2-hydroxyethyl)-1,4-cyclohexanediamine hydrochloride

DETD [1649] Cis-N-(5-isoquinolyl)-N'-(3-hydroxypropyl)-1,4-cyclohexanediamine hydrochloride

DETD [1652] Cis-N-(4-methyl-5-isoquinolyl)-N'-(2-hydroxyethyl)-1,4-cyclohexanediamine hydrochloride

DETD [1655] Cis-N-(4-methyl-5-isoquinolyl)-N'-(3-hydroxypropyl)-1,4-cyclohexanediamine hydrochloride

DETD [1658] Trans-1-[(4-cyano-5-isoquinolyl)oxy]-4-[(2-hydroxyethyl)amino]cyclohexane hydrochloride

DETD [1662] Trans-1-[(4-cyano-5-isoquinolyl)oxy]-4-[(3-hydroxypropyl)amino]cyclohexane hydrochloride

DETD [1665] 1-(2-Hydroxyethyl)-4-[(4-cyano-5-isoquinolyl)oxy]piperidine hydrochloride

DETD [1669] 1-(3-Hydroxypropyl)-4-[(4-cyano-5-isoquinolyl)oxy]piperidine hydrochloride

DETD [1673] Trans-N-(1-hydroxy-4-methyl-5-isoquinolyl)-4-cyclohexanediamine hydrochloride

DETD [1682] (Step E) Synthesis of trans-N-(1-hydroxy-4-methyl-5-isoquinolyl)-1,4-cyclohexanediamine hydrochloride

DETD [1693] Isoquinoline-5-sulfonyl chloride hydrochloride (33 g, prepared according to the method described in Japanese Patent Unexamined

Publication (Kokai) No. 57-200366) was added to dichloromethane. . .

DETD [1695] According to the method of Reference Example 2, a reaction was performed by using isoquinoline-5-sulfonyl chloride hydrochloride (20 g) and 1,3-propylenediamine (22.2 g) to obtain the title compound (16.3 g).

DETD [1697] According to the method of Reference Example 2, a reaction was performed by using isoquinoline-5-sulfonyl chloride hydrochloride (18.8 g) and 1,4-butylenediamine (25 g) to obtain the title compound (12.3 g).

DETD [1702] Dichloromethane (80 ml) and water (80 ml) were added with isoquinoline-5-sulfonyl chloride hydrochloride (8 g) and added with sodium hydrogencarbonate with vigorous stirring until pH of the aqueous layer became 5 to 6,. . .

DETD [1709] According to Reference Example 5, Step B, a reaction was performed by using isoquinoline-5-sulfonyl chloride hydrochloride (7.8 g) and Intermediate 56 (5.97 g) to obtain the title compound (11.36 g).

DETD [1716] According to Reference Example 5, Step B, a reaction was performed by using isoquinoline-5-sulfonyl chloride hydrochloride (10 g) and Intermediate 59 (8.96 g) to obtain the title compound (13.39 g).

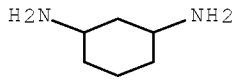
DETD [1723] According to Reference Example 5, Step B, a reaction was performed by using isoquinoline-5-sulfonyl chloride hydrochloride (9 g) and Intermediate 62 (8 g) to obtain the title compound (11.3 g).

IT 60-12-8, Phenethyl alcohol 100-09-4, 4-Anisic acid 107-19-7, 2-Propyn-1-ol 109-76-2, 1,3-Propanediamine 110-60-1, 1,4-Butanediamine 122-97-4, 3-Phenyl-1-propanol 539-48-0, 1,4-Benzenedimethanamine 610-94-6, Methyl 2-bromobenzoate 618-89-3, Methyl 3-bromobenzoate 619-42-1, Methyl 4-bromobenzoate 699-12-7, 2-(Phenylthio)ethanol 766-00-7, 2-Cyclopentylethanol 1196-39-0, 4-Methylisoquinoline 1477-55-0, 1,3-Benzenedimethanamine 1532-97-4, 4-Bromoisoquinoline 1875-88-3, 4-Chlorophenethyl alcohol 2393-23-9, 4-Methoxybenzylamine 2439-04-5, 5-Hydroxyisoquinoline 2615-25-0, trans-1,4-Cyclohexanediamine 2722-36-3, 3-Phenyl-1-butanol 3360-41-6, 4-Phenyl-1-butanol 3385-21-5, 1,3-Cyclohexanediamine 3466-32-8, 4-Bromophenyl methyl sulfone 5402-55-1, 2-(2-Thienyl)ethanol 7328-91-8, 2,2-Dimethyl-1,3-propanediamine 7589-27-7, 4-Fluorophenethyl alcohol 13781-67-4, 2-(3-Thienyl)ethanol 17739-45-6, 2-(2-Bromoethoxy)tetrahydro-2H-pyran 18203-70-8 19614-16-5, 2-Bromothioanisole 20611-21-6, 2-(Phenylsulfonyl)ethanol 24424-99-5, Di-tert-butyl dicarbonate 27489-62-9, trans-4-Aminocyclohexanol 33733-73-2, 3-Bromothioanisole 33821-94-2, 2-(3-Bromopropoxy)tetrahydro-2H-pyran 34784-04-8, 5-Bromoisoquinoline 38446-95-6, tert-Butyl 4-oxocyclohexanecarboxylate 50919-06-7 51644-96-3 57260-73-8, N-(2-Aminoethyl)carbamic acid tert-butyl ester 58142-97-5, 1-Chloro-5-nitroisoquinoline 58885-58-8, N-(3-Hydroxypropyl)carbamic acid tert-butyl ester 75178-96-0, N-(tert-Butoxycarbonyl)-1,3-propanediamine 79099-07-3, 1-(tert-Butoxycarbonyl)-4-oxopiperidine 84468-15-5, Isoquinoline-5-sulfonyl chloride 87120-72-7, 4-Amino-1-(tert-butoxycarbonyl)piperidine 90224-96-7 105627-79-0, 5-Isoquinolinesulfonyl chloride hydrochloride 108467-99-8 109384-19-2, 1-(tert-Butoxycarbonyl)-4-hydroxypiperidine 116574-71-1 127625-94-9 141519-77-9, 1-Chloro-5-isoquinolinesulfonyl chloride 144222-22-0, 4-(Aminomethyl)-1-tert-butoxycarbonylpiperidine 150349-36-3, N-(3-Aminopropyl)-N-methylcarbamic acid tert-butyl ester 184637-48-7, 3-Amino-1-(tert-Butoxycarbonyl)piperidine 194032-18-3
(preparation of isoquinoline derivs. as myosin regulatory light-chain phosphorylation inhibitors)

IT 3385-21-5, 1,3-Cyclohexanediamine
(preparation of isoquinoline derivs. as myosin regulatory light-chain phosphorylation inhibitors)

RN 3385-21-5 USPATFULL

CN 1,3-Cyclohexanediamine (CA INDEX NAME)



L79 ANSWER 21 OF 38 USPATFULL on STN

ACCESSION NUMBER:	2004:228019 USPATFULL Full-text
TITLE:	Methods and compounds for inhibitting MRP1
INVENTOR(S):	Kroin, Julian, Indianapolis, IN, UNITED STATES Norman, Bryan Hurst, Indianapolis, IN, UNITED STATES York, Jeremy Schulenburg, Indianapolis, IN, UNITED STATES

	NUMBER	KIND	DATE
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	NUMBER	DATE	
PRIORITY INFORMATION:	US 1999-171373P	19991222 (60)	<--
	US 2000-226076P	20000817 (60)	<--
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DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	ELI LILLY AND COMPANY, PATENT DIVISION, P.O. BOX 6288, INDIANAPOLIS, IN, 46206-6288
NUMBER OF CLAIMS:	71
EXEMPLARY CLAIM:	1
LINE COUNT:	12657

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention further relates to a method of inhibiting MRP1 in a mammal which comprises administering to a mammal in need thereof an effective amount of a compound of formula (I). ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD [0227] cxxxv. The compound is the hydrochloride salt.

DETD [0236] h) N-[3-(9-Chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-2-methylamino-acetamide hydrochloride

DETD [0239] k) 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-2-methyl-propionamide hydrochloride

DETD [0241] m) 2-Amino-N-[39-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-acetamide hydrochloride

DETD [0245] q) N-[349-Chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-2-phenyl-2-piperazin-1-yl-acetamide dihydrochloride

DETD [0247] s) N-[3-(9-Chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-2-methylamino-2-phenyl-acetamide hydrochloride

DETD [0260] ff) 1-Amino-cyclohexanecarboxylic acid [3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-S-yl)-cyclohexyl]-amide hydrochloride

DETD [0267] mm) 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-2-cyclohexyl-acetamide hydrochloride

DETD [0268] nn) 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-2-cyclohexyl-acetamide hydrochloride

DETD [0289] iii) N-[3-(9-Chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclopentyl]-2-methylamino-acetamide hydrochloride

DETD [0292] lll) 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclopentyl]-2-methyl-propionamide hydrochloride

DETD [0294] nnn) 2-Amino-N-[3-(9-chloro-3-methyl oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclopentyl)-acetamide hydrochloride

DETD [0298] rrr) N-(3-(9-Chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclopentyl]-2-phenyl-2-piperazin-1-yl-acetamide dihydrochloride

DETD [0300] ttt) N-[3-(9-Chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclopentyl]-2-methylamino-2-phenyl-acetamide hydrochloride

DETD [0313] gggg) 1-Amino-cyclohexanecarboxylic acid [3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclopentyl]-amide hydrochloride

DETD [0320] nnnn) 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclopentyl]-2-cyclohexyl-acetamide hydrochloride

DETD [0321] oooo) 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-2-cyclopentyl-acetamide hydrochloride

DETD [0381] For compounds in which het is pyrazole, the addition of 1-(3-dimethyl-aminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) to the reaction is preferred. The compound of formula XI is preferably the corresponding carboxylic acid and is employed. . .

DETD . . . of formula XIII by dissolving or suspending a compound of formula XVI in a suitable acidic solvent and adding hydroxylamine hydrochloride. Glacial acetic acid is a convenient acidic solvent and is typically preferred. The ester group is then hydrolyzed to the. . .

DETD [0396] Generically, the compound of formula XVIII and hydroxylamine hydrochloride are suspended or dissolved in a suitable solvent and a suitable base is added. After the reaction is complete, the. . .

DETD [0472] To a suspension of 5.00 g (26.5 mmol) of 3-nitrobenzylamine hydrochloride in 100 mL CH.sub.2Cl.sub.2 at room temperature was added 5.79 g (26.5 mmol) of di-t-butyl dicarbonate. To this was added. . .

DETD 5-((3S,1R)-3-Aminocyclohexyl)-9-chloro-3-methyl-5H-isoxazolo[4,3-c]quinolin-4-one hydrochloride

DETD 5-((1S,3R)-3-aminocyclohexyl)-9-chloro-3-methyl-5H-isoxazolo[4,3-c]quinolin-4-one hydrochloride

DETD . . . the resulting solid dried overnight in vacuo which resulted in the isolation of 6.84 g (94%) of the desired ester hydrochloride. MS(ES): (M+1)+172.2 m/z.

DETD . . . a gas. After stirring the resulting solution for 30 min, triethyl amine (746 μL; 5.36 mmol; 2 equiv) and N,O-dimethylhydroxylamine hydrochloride (570 mg; 5.90 mmol; 2.2. equiv) were added and the solution stirred for 15 h. Water was added to the. . .

DETD 4-Amino-1-ethylcyclohexanecarboxylate hydrochloride

DETD trans-5-[3-(Aminomethyl)cyclohexyl]-9-chloro-3-methyl-5H-isoxazolo[4,3-c]quinolin-4-one hydrochloride

DETD . . . preparation 147 (16.9 g, 67.6 mmol) in H.sub.2O (35 mL), EtOH (35 mL), and ice (25 g) was added hydroxylamine hydrochloride (4.8 g, 74.4 mmol). Then, 169 mmol of 50% NaOH (6.76 g in 6.76 mL H.sub.2O) was added with stirring.. . .

DETD N-t-Butyl-N'-(2-chloro-6-fluorobenzylidene)hydrazine hydrochloride

DETD [0581] A mixture of t-butyl hydrazine hydrochloride (1.24 g, 10 mmol) and 2-chloro-6-fluorobenzaldehyde (1.1 mL, 10 mmol) dissolved in acetic acid (5 mL) was stirred at 50°. . .

DETD Cis-3-(amino)-1-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexane hydrochloride

DETD 3-(2-Amino-trans-cyclohexyl)propionic acid methyl ester hydrochloride

DETD 3-(2-Amino-cis-cyclohexyl)propionic acid methyl ester hydrochloride
DETD Methyl 3-(2-aminocyclohexyl)propanoate hydrochloride
DETD 4-Methoxypicolinic acid hydrochloride
DETD . . . in 120 mL of tetrahydrofuran was added 12 mL (88.0 mmol) of triethylamine and 5.4 g (66.0 mmol) of dimethylamine hydrochloride. The reaction mixture was heated at 60° C. in a sealed tube for three hours, cooled to ambient temperature and. . .
DETD [0740] Benzoyl chloride (1.40 mL, 12.1 mmol) was added in a dropwise manner to a mixture of L-proline methyl ester hydrochloride (2.00 g, 12.1 mmol) and Et.sub.3N (4.20 mL, 30.2 mmol) in CH.sub.2Cl.sub.2 (40 mL) and the resulting mixture stirred overnight. . .
DETD [0742] Phenacetyl chloride (1.60 mL, 12.1 mmol) was added to a mixture of L-proline methyl ester hydrochloride (2.00 g, 12.1 mmol) and Et.sub.3N (4.20 mL, 30.2 mmol) in CH.sub.2Cl.sub.2 (40 mL) and the resulting mixture stirred overnight. . .
DETD . . . acid ethyl ester (2.54 g; 10.2 mmol) was reacted in a sealed tube, at rt., in CH.sub.2Cl.sub.2, overnight with N,N-dimethylamine hydrochloride (3.34 g; 41.0 mmol; 4 equiv) and Et.sub.3N (5.8 mL; 41.0 mmol; 4 equiv). The reaction solution was evaporated to. . .
DETD [0782] To a suspension of 5.00 g (26.5 mmol) of 3-nitrobenzylamine hydrochloride in 100 mL CH.sub.2Cl.sub.2 at rt. was added 5.79 g (26.5 mmol) of di-t-butyl dicarbonate. To this was added 8.13. . .
DETD 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-acetamide hydrochloride
DETD . . . solution of a compound from preparation 377 (0.05 g, 0.13 mmol) in acetic acid (5 mL) was treated with hydroxylamine hydrochloride (13 mg, 0.19 mmol). The solution was heated to reflux and stirred 5 hr. The reaction was then diluted in. . .
DETD . . . (M+)

carboxamide		
415	N-[(1R,3S)-3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]-quinolin-5-yl)cyclohexylmethyl]-2-(1-methyl-1H-imidazol-4-yl)acetamide	1-methyl-4-imidazole acetic acid hydrochloride
Ex 615	MS (ion spray) 468 (M.sup.+), 466 (M.sup.- - 1)	
416	3-Benzoyl-N-[(1R,3S)-3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexylmethyl]-benzamide	3-benzoylbenzoic acid
Ex 615	MS (ion spray) 554 (M.sup.+), 552 (M.sup.- - 1)	
417	N-[(1R,3S)-3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-	3-
Ex 615. . .		

DETD . . . the combined extracts were dried over sodium sulfate. Concentration in vacuo left the crude acid which was combined with 1-(3-dimethyl-aminopropyl-3-ethylcarbodiimide hydrochloride (0.186 g, 0.00097 mol), 1-hydroxy-7-azabenzotriazole (0.133 g, 0.00098 mol) and 3,4,5-trimethoxybenzylamine (0.193 g, 0.00098 mol) in DMF (15 mL) and. . .
DETD . . . To a solution of the compound from Example 490 in denatured ethanol (6 mL) was added a solution of methoxyamine hydrochloride (74.5 mg; 0.892 mmol; 4 equiv) and sodium acetate (73.1 mg; 0.892 mmol; 4 equiv) in water (1 mL). The. . .
DETD (1S,3R)-1-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-3-[((2S)-2-amino-2-phenylacetyl)amino]cyclohexane hydrochloride
DETD (1R,3S)-1-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-3-[((2S)-2-amino-2-phenylacetyl)amino]cyclohexane hydrochloride

DETD (1S,3R)-1-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-3-[((2R)-2-amino-2-phenylacetyl) amino]cyclohexane hydrochloride

DETD . . . mL of N,N-dimethylformamide. To this solution was added 23 mg (0.17 mmol) of 1-hydroxy-7-azabenzotriazole, 33 mg (0.17 mmol) of 1-(3-dimethyl-aminopropyl)-3-ethylcarbodiimide hydrochloride, 5 mg of 4-dimethylaminopyridine and 60 μL (0.42 mmol) of triethylamine. Yield=33 mg (53%) of the desired isomer as a. . .

DETD 1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid [3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexyl]amide hydrochloride

DETD 1,2,3,4-Tetrahydro-isoquinoline-3-carboxylic acid [3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-amide hydrochloride

DETD 2-Amino-N-{[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexylcarbamoyl]-phenylmethyl}-2-methylpropionamide hydrochloride

DETD [0930] A compound from Example 321 was deprotected in a manner similar to Example 638 and kept as the hydrochloride salt. MS(ES) calc'd: [M+H].sup.+=550.2 m/z; [M-H].sup.-=548.2 m/z; [M+Cl].sup.-=584.2 m/z. Found: 550.0 m/z; 548.0 m/z; 584.0 m/z.

DETD [0935] A solution of N-{[3-(3-acetylamino-5-chloro-2-oxohydroquinolyl)-cyclobexyl]-methyl}(phenylmethoxy)carboxamide (0.02 g, 0.04 mmol) in acetic acid (2 mL) was treated with hydroxylamine hydrochloride (3 mg, 0.046 mmol). The solution was heated to reflux and stirred 4 hr. The reaction was then diluted in. . .

DETD [0937] A solution of N-{[3-(3-acetylamino-5-chloro-2-oxohydroquinolyl)cyclohexyl]-methyl}(6-fluoro(3-pyridyl))carboxamide (0.035 g, 0.07 mmol) in acetic acid (5 mL) was treated with hydroxylamine hydrochloride (7.8 mg, 0.11 mmol). The solution was heated to reflux and stirred 3 hr. The reaction was then diluted in. . .

DETD N-[3-(9-Chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-2-methylamino-acetamide hydrochloride

DETD 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexyl]-2-methyl-propionamide hydrochloride

DETD 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-SH-isoxazolo[4,3-c]quinolin-5-yl)cyclohexyl]-acetamide hydrochloride

DETD N-[3-(9-Chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexyl]-2-phenyl-2-piperazin-1-ylacetamide dihydrochloride

DETD N-[3-(9-Chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexyl]-2-methylamino-2-phenylacetamide hydrochloride

DETD 1-Aminocyclohexanecarboxylic acid [3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexyl]amide hydrochloride

DETD 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexyl]-2-cyclohexylacetamide hydrochloride

DETD 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexyl]-2-cyclohexylacetamide hydrochloride

DETD 2-Aminoindan-2-carboxylic acid [3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexyl]amide hydrochloride

DETD 1-Amino-cyclopentanecarboxylic acid [3-(9-chloro-3-methyl-4-oxo-4H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-amide hydrochloride

DETD 1-Amino-cyclopropanecarboxylic acid (3-(9-chloro-3-methyl oxo-4H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-amide hydrochloride

DETD R(-)Amino-acetic acid [3-(9-chloro-3-methyloxo-4H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexylcarbamoyl]-phenyl-methyl ester hydrochloride

DETD S(+)Amino-acetic acid [3-(9-chloro-3-methyl-4-oxo-4H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexylcarbamoyl]-phenyl-methyl ester hydrochloride

DETD . . . mg, 0.25 mmol), 1-hydroxy-7-azabenzo-triazole (34 mg, 0.25 mmol), N,N-diisopropylethyl amine (0.10 mL, 0.58 mmol), DMAP (5 mg, cat.), and N-benzylglycine hydrochloride (50 mg, 0.25 mmol) in DMF(6 mL) and the mixture stirred overnight at rt. The mixture was then concentrated in. . . EtOAc and treated with excess diethyl ether/hydrochloric acid. Concentration of this mixture to dryness

allowed for quantitative recovery of the hydrochloride salt as an off white solid. MS(ES): (M+1)+479.1, 481.2.

DETD . . . 638 (50 mg; 0.108 mmol) was dissolved in anhydrous dimethylformamide (10 mL) under a nitrogen atmosphere, mixed with 1-methyl-piperidine-4-carboxylic acid hydrochloride (58.0 mg; 0.323 mmol; 3 equiv), 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (61.8 mg; 0.323 mmol; 3 equiv), 2,4,6-trimethylpyridine (86 μL; 0.645 mmol; 6 equiv), and 1-hydroxy-7-azabenzotriazole (43.9 mg; 0.323 mmol; 3. . .

DETD . . . one (50 mg; 0.151 mmol), N-phenylglycine (29.6 mg; 0.196 mmol; 1.3 equiv), 1-hydroxy-7-azabenzotriazole (26.7 mg; 0.196 mmol; 1.3 equiv), 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (37.6 mg; 0.196 mmol; 1.3 equiv), and 2,4,6-trimethylpyridine (199 μL; 1.51 mmol; 10 equiv). After overnight stirring at room temperature,. . .

DETD . . . of material from Preparation 210 (100 mg; 0.301 mmol) in anhydrous DMF. Diisopropylethylamine (262 μL; 0.392 mmol; 5 equiv), 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (75.1 mg; 0.392 mmol; 1.3 equiv), and 1-hydroxy-7-azabenzotriazole (53.3 mg; 0.392 mmol; 1.3 equiv) were then added and the solution. . .

DETD . . . methyl amide (700 mg, 2.0 mmol) in 35 mL of dichloromethane was added 440 mg (2.4 mmol) of nicotinoyl chloride hydrochloride, 0.85 mL (6.0 mmol) of triethylamine and 5 mg of 4-dimethylaminopyridine. The reaction mixture was stirred overnight at ambient temperature,. . .

DETD . . . triethylamine, 43 mg (0.27 mmol) of 6-chloronicotinic acid, 36 mg (0.27 mmol) of 1-hydroxy-7-azabenzo-triazole, 51 mg (0.27 mmol) of 1-(3-dimethylamino-propyl).sub.3-ethyl-carbodiimide hydrochloride and 5 mg of 4-dimethylaminopyridine. The reaction mixture was stirred overnight at ambient temperature and concentrated to dryness. The residue. . .

IT 52-52-8, 1-Amino-1-cyclopentanecarboxylic acid 55-22-1, Pyridine-4-carboxylic acid, reactions 59-67-6, Pyridine-3-carboxylic acid, reactions 62-53-3, Aniline, reactions 69-72-7, Salicylic acid, reactions 75-64-9, tert-Butylamine, reactions 76-93-7, reactions 79-14-1, Glycolic acid, reactions 79-30-1, Isobutyryl chloride 87-62-7, 2,6-Dimethylphenylamine 90-04-0, 2-Methoxyphenylamine 90-52-8, 6-Methoxyquinolin-8-ylamine 92-54-6, 1-Phenylpiperazine 93-97-0, Benzoic anhydride 95-53-4, 2-Methylphenylamine, reactions 95-55-6, 2-Aminophenol 96-50-4, 2-Aminothiazole 98-09-9, Benzenesulfonyl chloride 98-88-4, Benzoyl chloride 98-97-5, 2-Pyrazinecarboxylic acid 98-98-6, Pyridine-2-carboxylic acid 99-03-6 99-59-2, 2-Methoxy-5-nitroaniline 100-07-2, 4-Methoxybenzoyl chloride 100-46-9, Benzylamine, reactions 100-51-6, Benzyl alcohol, reactions 100-53-8, Benzyl mercaptan 100-60-7, N-Methyl-N-cyclohexylamine 100-61-8, N-Methylaniline, reactions 103-49-1, Dibenzylamine 103-67-3, N-Methyl-N-benzylamine 103-71-9, Phenyl isocyanate, reactions 103-72-0, Phenyl thioisocyanate 103-76-4, 1-(2-Hydroxyethyl)piperazine 103-80-0, Phenacetyl chloride 103-82-2, Phenylacetic acid, reactions 104-01-8 104-94-9, 4-Methoxyphenylamine 106-49-0, 4-Methylphenylamine, reactions 108-40-7, 3-Methylthiophenol 108-44-1, 3-Methylphenylamine, reactions 108-91-8, Cyclohexylamine, reactions 108-98-5, Thiophenol, reactions 109-00-2, 3-Hydroxypyridine 109-01-3, 1-Methylpiperazine 110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions 121-90-4, 3-Nitrobenzoyl chloride 121-91-5, Isophthalic acid, reactions 122-01-0, 4-Chlorobenzoyl chloride 122-04-3, 4-Nitrobenzoyl chloride 123-75-1, Pyrrolidine, reactions 123-90-0, Thiomorpholine 124-68-5, 2-Amino-2-methyl-1-propanol 134-32-7, 1-Naphthylamine 142-08-5, 2-Hydroxypyridine 329-15-7, 4-Trifluoromethylbenzoyl chloride 331-25-9 348-52-7,

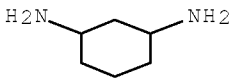
1-Fluoro-2-iodobenzene 348-54-9, 2-Fluoroaniline 360-03-2 371-40-4, 4-Fluoroaniline 371-42-6, 4-Fluorothiophenol 372-19-0, 3-Fluoroaniline 372-39-4, 3,5-Difluoroaniline 387-45-1, 2-Chloro-6-fluorobenzaldehyde 393-52-2, 2-Fluorobenzoyl chloride 393-55-5, 2-Fluoronicotinic acid 395-35-7, p-Trifluoromethylmandelic acid 402-65-3, 2-Fluoroisonicotinic acid 402-66-4, 5-Fluoronicotinic acid 403-43-0, 4-Fluorobenzoyl chloride 403-45-2, 6-Fluoronicotinic acid 405-50-5 407-22-7, 2-Fluoro-6-methylpyridine 434-75-3, 2-Chloro-6-fluorobenzoic acid 446-52-6, o-Fluorobenzaldehyde 462-08-8, 3-Aminopyridine 467-69-6, 9-Hydroxy-9-fluorenecarboxylic acid 486-74-8, Quinoline-4-carboxylic acid 498-95-3, Nipecotic acid 500-22-1, 3-Pyridinecarboxaldehyde 501-53-1 501-81-5, 2-(3-Pyridyl)acetic acid 501-97-3, 3-(4-Hydroxyphenyl)propionic acid 504-24-5, 4-Aminopyridine 504-29-0, 2-Aminopyridine 527-69-5, 2-Furoyl chloride 536-90-3, 3-Methoxyaniline 552-63-6, DL-Tropic acid 573-03-5, 4-Fluoro-1-naphthoic acid 579-18-0, 3-Benzoylbenzoic acid 583-08-4, Nicotinuric acid 586-75-4, 4-Bromobenzoyl chloride 591-27-5, 3-Aminophenol 594-61-6, 2-Methyllactic acid 603-80-5, 2-Methyl-3-hydroxybenzoic acid 609-65-4, 2-Chlorobenzoyl chloride 611-71-2, D-(-)-Mandelic acid 611-73-4, Benzoylformic acid 611-95-0, 4-Benzoylbenzoic acid 612-41-9, 2-Nitrocinnamic acid 612-62-4, 2-Chloroquinoline 615-18-9, 2-Chlorobenzoxazole 615-20-3, 2-Chlorobenzothiazole 618-46-2, 3-Chlorobenzoyl chloride 619-45-4, 4-Aminobenzoic acid methyl ester 620-23-5 626-58-4, 4-Methylpiperidine 626-64-2, 4-Hydroxypyridine 638-29-9, Valeryl chloride 645-45-4, Hydrocinnamoyl chloride 684-07-1 701-97-3, Cyclohexanepropionic acid 765-30-0, Cyclopropylamine 771-50-6, Indole-3-carboxylic acid 824-94-2, p-Methoxybenzyl chloride 826-55-1 830-96-6, 1H-Indole-3-propanoic acid 874-60-2, 4-Methylbenzoyl chloride 879-18-5, Naphthalene-1-carbonyl chloride 930-68-7, 2-Cyclohexen-1-one 933-88-0, 2-Methylbenzoyl chloride 934-60-1, 6-Methylpicolinic acid 951-82-6, 3,4,5-Trimethoxyphenylacetic acid 955-40-8, N-Benzyl-L-proline ethyl ester 1003-03-8, Cyclopentylamine 1118-68-9, N,N-Dimethylglycine 1120-88-3, 4-Methylpyridazine 1121-60-4, 2-Pyridinecarboxaldehyde 1122-96-9, 4-Methoxypyridine N-oxide 1129-28-8, Methyl 3-(bromomethyl)benzoate 1135-67-7 1148-11-4, N-Carbobenzyloxy-L-proline 1477-50-5, Indole-2-carboxylic acid 1578-63-8, .α.-Fluorophenylacetic acid 1710-98-1, 4-tert-Butylbenzoyl chloride 1711-02-0, 4-Iodobenzoyl chloride 1711-05-3, 3-Methoxybenzoyl chloride 1711-06-4, 3-Methylbenzoyl chloride 1711-07-5, 3-Fluorobenzoyl chloride 1711-09-7, 3-Bromobenzoyl chloride 1776-53-0, 4-Amino-1-cyclohexanecarboxylic acid 1798-09-0, 3-Methoxyphenylacetic acid 1821-12-1, 4-Phenylbutyric acid 1877-73-2, 3-Nitrophenylacetic acid 1885-14-9, Phenyl chloroformate 1912-48-7, 1-Methyl-3-indoleacetic acid 1918-77-0, 2-Thiopheneacetic acid 1939-99-7, .α.-Toluenesulfonyl chloride 2051-95-8, 3-Benzoylpropionic acid 2124-55-2, Indole-4-carboxylic acid 2133-40-6, L-Proline methyl ester hydrochloride 2215-77-2, 4-Phenoxybenzoic acid 2243-83-6, Naphthalene-2-carbonyl chloride 2251-65-2, 3-Trifluoromethylbenzoyl chloride 2392-54-3 2398-81-4, Nicotinic acid N-oxide 2516-34-9, Cyclobutylamine 2557-77-9, 3-Fluorothiophenol 2719-27-9, Cyclohexylcarbonyl chloride 2756-85-6, 1-Amino-1-cyclohexanecarboxylic acid 2768-42-5 2900-27-8 2935-35-5 2975-41-9, 2-Aminoindan 3128-05-0, 3-Oxocyclopentaneacetic acid 3173-56-6, Benzyl isocyanate 3222-47-7, 6-Methylnicotinic acid 3222-49-9, 5-Methylnicotinic acid 3222-56-8, 2-Methylnicotinic acid 3262-72-4 3282-30-2, Pivaloyl chloride 3385-21-5, 1,3-Diaminocyclohexane 3441-03-0, Methyl 3-(chlorocarbonyl)benzoate 3535-37-3, 3,4-Dimethoxybenzoyl chloride 3622-23-9, 2,6-Dichlorobenzothiazole 3684-12-6 3724-19-4, 3-(3-Pyridyl)propionic

acid 3731-52-0, 3-(Aminomethyl)pyridine 3739-38-6, 3-Phenoxybenzoic acid 3863-11-4, 3,4-Difluoroaniline 3934-20-1, 2,4-Dichloropyrimidine 3966-30-1 3966-32-3 4100-13-4, 1,2,3-Thiadiazole-4-carboxylic acid 4110-80-9 4341-76-8, Ethyl 2-butynoate 4521-61-3, 3,4,5-Trimethoxybenzoyl chloride 4530-20-5, N-tert-Butoxycarbonylglycine 4595-59-9, 5-Bromopyrimidine 4595-60-2, 2-Bromopyrimidine 4684-94-0, 6-Chloro-2-pyridinecarboxylic acid 4755-50-4, 4-Dimethylaminobenzoyl chloride 4870-65-9, .α.-Bromophenylacetic acid 5006-22-4, Cyclobutylcarbonyl chloride 5166-67-6, Ethyl 1-methylnipecotate 5271-67-0, 2-Thiophenecarbonyl chloride 5326-23-8, 6-Chloronicotinic acid 5382-16-1, 4-Hydroxypiperidine 5398-44-7, 2,6-Dichloroisonicotinic acid 5426-55-1 5452-35-7, Cycloheptylamine 5470-22-4, 4-Chloropicolinic acid 5720-07-0, 4-Methoxyphenylboronic acid 5813-64-9, Neopentylamine 6064-63-7, 2-Hydroxycaproic acid 6068-72-0, 4-Cyanobenzoyl chloride 6120-95-2 6313-54-8, 2-Chloroisonicotinic acid 6342-19-4 6368-20-3 6404-31-5, N-Carbobenzyloxy-D-proline 6419-36-9, 3-Pyridylacetic acid hydrochloride 6480-68-8, 3-Quinolinecarboxylic acid 6602-54-6 6622-91-9, 4-Pyridylacetic acid hydrochloride 6921-34-2, Benzylmagnesium chloride 6973-60-0, N-Methylpyrrole-2-carboxylic acid 7021-09-2, 2-(2-Methoxyphenyl)acetic acid 7031-23-4, 3-Methylthiopropionyl chloride 7322-88-5, (S)-(+)-O-Acetylmandelic acid 7326-19-4, D-3-Phenyllactic acid 7377-26-6, Methyl 4-(chlorocarbonyl)benzoate 7400-27-3, tert-Butyl hydrazine hydrochloride 7418-65-7, 4-Aminonicotinic acid 7472-67-5 7782-24-3, (S)-(+)-2-Phenylpropionic acid 7782-26-5 7785-26-4 10002-29-6 10333-11-6 10351-19-6, (4-Pyridylthio)acetic acid 10400-19-8, Nicotinoyl chloride 10490-07-0 10502-44-0, p-Methoxymandelic acid 10541-83-0, 4-(Methylamino)benzoic acid
(preparation of N-isoxazoloquinolinylcyclohexylcarboxamides and analogs as MRP1 inhibitors)

IT 3385-21-5, 1,3-Diaminocyclohexane
(preparation of N-isoxazoloquinolinylcyclohexylcarboxamides and analogs as MRP1 inhibitors)

RN 3385-21-5 USPATFULL

CN 1,3-Cyclohexanediamine (CA INDEX NAME)



L79 ANSWER 22 OF 38 USPATFULL on STN

ACCESSION NUMBER: 2004:216220 USPATFULL Full-text

TITLE: Synthesis of macrocyclic tetraamido compounds and new metal insertion process

INVENTOR(S): Horwitz, Colin P., Pittsburgh, PA, UNITED STATES
Ghosh, Anindya, Pittsburgh, PA, UNITED STATES

	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 2004167329	A1	20040826		
	US 7060818	B2	20060613		
APPLICATION INFO.:	US 2003-371591	A1	20030221	(10)	<--

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: KIRKPATRICK & LOCKHART LLP, 535 SMITHFIELD STREET, PITTSBURGH, PA, 15222
NUMBER OF CLAIMS: 73
EXEMPLARY CLAIM: 1
LINE COUNT: 1808
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An improved method of synthesizing a macrocyclic tetraamido compound includes protecting the amino portion of an amino carboxylic acid to form a protected amino carboxylic acid; exposing the protected amino carboxylic acid to a first solvent, preferably a hydrocarbon solvent, such as toluene or 1,2-dichloroethane, dichloromethane, dibromomethane and 1,2-dibromoethane. The carboxylic acid portion of the protected amino carboxylic acid is then converted to an activated carboxylic acid by one of esterification or acid halide formation, to form a protected amino activated carboxylic acid derivative. The protected amino activated carboxylic acid derivative is reacted with a diamine in the presence of a second solvent, such as THF or ,2-dichloroethane, dichloromethane, dibromomethane and 1,2-dibromoethane, to form a protected diamide diamine intermediate. Following deprotection, the diamide diamine intermediate is reacted with an activated diacid, such as an activated malonate, oxalate or succinate derivative to form the macrocyclic tetraamido compound. The macrocyclic tetraamido compound may further be complexed with a transition metal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . Ornithine
Tyrosine
Cysteine
Lysine
Arginine
Histidine
asparagine (aspartic acid)
glutamine (glutamic acid)
phenylalanine (L-α-amino-β-phenyl propionic acid)
Other Amino Acids
(S)-2-amino-3-methoxypropionic acid
α-amino-β-methylaminopropionic acid hydrochloride
R(-)-2-amino-2-methyl butanedioic acid
S(+)-2-amino-2-methyl butanedioic acid
S(+)-2-amino-2-methyl butanoic acid hydrate
2-amino-2-methyl butyric acid. . . oleic acid
L-2-amino-4-pentenoic acid (L-C-allyl glycine)
2-amino-3-phenylbutanoic acid
DL-2-amino-4-phenylbutyric acid
β-cyanoalanine
Homocysteine
Azaserine
S-adenosylmethionine
citrulline
(L-2-amino-5-ureidovaleric acid)
α-aminohydrocinnamonitrile
L-2-amino-4-hydroxy butyric acid
3-methyl
hydroxy-4-methyl
hydroxy-valeric acid
R(-)-α-aminophenyl acetic acid (D(-)-α-phenylbutyric acid
ureidopropionic acid (albizzin)
phenylthiobutanoic acid
(R,S)-2-amino-3-hydroxy-butanoic acid
(2S,3R)-2-amino-3-pentanoic acid
DL-α-amino-β-phenyl glycine)
R(-)-2-amino-2-
L-2-amino-3-
(2R,3S)-2-amino-3-hydrochloride

DL-2-aminovaleric acid (DL-norvaline)
DL-2-amino-5-phosphono pentanoic acid (DL-2-amino-5-phosphono valeric acid)
D(-)-2-amino-4-phosphonobutyric acid
D(-)-2-amino-3-phosphono. . . acid
DL-α-amino-3-thiopheneacetic acid
2-amino-4,4,4-trifluorobutyric acid
2-aminostearic acid
DL-2-amino suberic acid
L(+)-2-amino-6-(O,O'-Diethylphosphono)hexanoic acid ethoxy butanoic
L-2-amino-4-sulfamoyl butyric acid
L-2-amino-3-sulfamoyl propionic acid
DL-2-amino-7-sulfoheptanoic acid
D-α-amino adipic acid
L-α-amino adipic. . .
L(+)-2-amino-4-phosphonobutyric acid
L(+)-2-amino-5-phosphono valeric acid)
cis(+/-)-1-amino-3-phosphono cyclohexane carboxylic acid
1-aminocyclopentane-1-carboxylic acid (cycloleucine)
1-aminocyclohexane-1-carboxylic acid
2-aminodecanoic acid
α-amino succinic acid
(2S,3S)-2-amino-3-ethoxy butanoic acid hydrochloride
2-amino-3-fluoro butyric acid
L-α-amino-γ-guanidino butyric acid
L-α-amino-β-guanidino propionic acid
2-amino heptanoic acid

DETD . . . 3,5-dimethyl-

Registry #	Other β-amino carboxylic acids
15540-91-7	3,6-dimethyl-
2789-92-6	3,5-dichloro-
609-85-8	3,5-dibromo-
	3,5-dibromo-6-fluoro-
118-92-3	(o-amino-benzoic acid, anthranilic acid)
3177-80-8	3-methoxy-
6705-03-9	5-methoxy-
394-31-0	5-hydroxy-
4920-81-4	3-hydroxy-hydrochloride
446-32-2	4-fluoro-
446-08-2	5-fluoro-
434-76-4	6-fluoro-
	4-chloro-5-sulfamoyl-
6388-47-2	3-chloro-
89-77-0	4-chloro-
635-21-2	5-chloro-
2148-56-3	6-chloro-
	3-bromo-5-methyl-
1765-42-0	3,4,5,6-tetrafluoro-
61948-85-4	3,4,5-trimethoxy-
	3-amino-5-phenylthiophene-carboxamide
5434-20-8	3-amino-pthalic acid
627-95-2	β-amino-valeric acid hydrochloride

	2-amino-4-methyl-thiophene-3-carboxamide
	2-amino-5-methyl-thiophene-3-carboxamide
1068-84-4	amino-malonic acid
614-19-7	β-amino-hydrocinnamic acid (D,L-3-amino-3-phenyl-propionic acid)
4507-13-5	2-amino-5-ethylthiophene-3-carboxylic acid, ethyl ester
52834-01-2	2-amino-4,6-dimethyl-3-pyridinecarboxylic acid hydrochloride
54711-21-6	5-amino-4-cyano-1-methyl-pyrazole
698-29-3	4-amino-5-cyano-2-methyl pyrimidine
	4-amino-5-cyano-2-methoxy pyrimidine
16750-40-6	3-amino-butyronitrile
82-24-6	1-aminoanthraquinone-2-carboxylic acid
107-95-9	3-amino-propionic acid (β alanine)
41680-34-6	3-aminopyrazole-4-carboxylic acid
. . . acid	
5345-47-1	2-amino-nicotinic acid (2-aminopyridine-3-carboxylic acid)
82-24-6	1-amino-anthraquinone-2-carboxylic acid
1664-54-6	3-amino-3-phenyl-propionic acid
50427-77-5	5-amino-1-phenylpyrazole-4-carboxamide
72-40-2	5(4)-aminoimidazole-4(5)-carboxamide hydrochloride
2627-69-2	5-amino-4-imidazole carboxamide riboside
68302-09-0	2-amino-7-ethyl-5-oxo-5H-[1]benzopyrano[2,3-b] pyridine-3-carbonitrile
22603-53-8	2-amino-3,5-dinitrobenzonitrile
	5-amino-4-cyano-1-(4-chlorophenyl)pyrazole
	5-amino-4-cyano-1-(4-nitrophenyl)pyrazole
16617-46-2	5-amino-4-cyano pyrazole
21112-45-8	β-amino-crotonic. . .
DETD . . . 3240-72-0	4,5-diamino-uracil (5,6-diamino-uracil)

Derivatives of n,n + 2 Diamines (6aa)

Registry #	n,n + 2-diamines
4403-69-4	2-amino-benzylamine
	2-amino-2-(2-aminophenyl)-propane
109-76-2	1,3-diaminopropane
3385-21-5	1,3-diaminocyclohexane
	1,3-diamino-1,3-dimethylcyclohexane
	2,4-diamino-2,4-dimethyl-pentane-3-one
	2,4-diamino-2,4-dimethyl-

pentane
479-27-6 1,8-diaminonapthalene
589-37-7 1,3-diaminopentane
7328-91-8 1,3-diamino-2,2-dimethyl propane

DETD . . . comprised of the protected diamide diamine intermediate, alcohol, such as absolute ethanol, and a hydrazine based reagent, such as hydrazine dihydrochloride. A base may be additionally added for some hydrazine based reagents, but is not necessary for all. The solution is. . . 10. Where hydrazine hydrate is added, for example, no additional base is needed. For hydrazine based reagents, such as hydrazine dihydrochloride or hydrazine acetate, for example, a pH of 10 or greater is desirable. The diamide diamine intermediate is extracted.

DETD . . . protected diamide diamine does not form the thick paste that it does, for example, in a toluene/THF mixture (the triethylammonium hydrochloride [Et.sub.3NH]Cl is partially soluble in 1,2-dichlorethane).

DETD [0117] The protected diamide diamine (3200 gm, 5.95 mol), absolute ethanol (23 L), and hydrazine dihydrochloride (1376 gm. 13.1 mol) were charged to a flask. The slurry was warmed to 30° C. and then triethylamine (2633. . .

DETD . . . was decanted from the solid. Methanol (55 L) was then charged to the reactor in order to dissolve the triethylammonium hydrochloride. The solution was mixed for 15 min and then the solid was allowed to settle. The methanol (64 L) was. . .

DETD . . . placed in a round bottom flask fitted with a reflux condenser, and 100 mL of absolute ethanol was added. Hydrazine dihydrochloride (2.9 g, 30.8 mmol) was added and the solution was warmed a few minutes then triethylamine (7.7 mL, 61.6 mmol). . .

DETD . . . placed in a round bottom flask fitted with a reflux condenser, and 250 mL of absolute ethanol was added. Hydrazine dihydrochloride (18.2 g, 187 mmol) was added and the solution was warmed a few minutes then triethylamine (48 mL, 374 mmol). . .

CLM What is claimed is:

30. The method recited in claim 28 wherein the hydrazine based reagent is one of hydrazine dihydrochloride or hydrazine acetate and the base is added and the pH is adjusted to greater than or equal to 10.
. . .

70. The method recited in claim 68 wherein the hydrazine based reagent is one of hydrazine dihydrochloride or hydrazine acetate and the base is added and the pH is adjusted to greater than or equal to 10.
. . .

L79 ANSWER 23 OF 38 USPATFULL on STN
ACCESSION NUMBER: 2004:179116 USPATFULL Full-text
TITLE: Rho kinase inhibitors
INVENTOR(S): Imazaki, Naonori, Suita, JAPAN
Kitano, Masafumi, Takatsuki, JAPAN
Ohashi, Naohito, Takatsuki, JAPAN
Matsui, Kazuki, Sanda, JAPAN

	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 2004138286	A1	20040715		
	US 7199147	B2	20070403		
APPLICATION INFO.:	US 2003-480526	A1	20031212	(10)	<--
	WO 2002-JP5609		20020606		<--

	NUMBER	DATE

PRIORITY INFORMATION: JP 2001-176826 20010612 <--
JP 2001-398992 20011228 <--
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: SUGHRUE MION, PLLC, 2100 PENNSYLVANIA AVENUE, N.W., SUITE 800, WASHINGTON, DC, 20037
NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Page(s)
LINE COUNT: 12676
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A compound represented by the formula (1): ##STR1##

wherein R.sup.1--X-- indicates that 1 to 4 R.sup.1--X-- groups are present which may be the same or different,

the ring A is a saturated or unsaturated 5-membered heterocyclic ring,

X is a single bond, a group represented by the formula: --N(R.sup.3)--, --O-- or --S--, or the like.

R.sup.1 is a hydrogen atom, a halogen atom, a nitro group, a carboxyl group, a substituted or unsubstituted alkyl group, or the like,

R.sup.2 is a hydrogen atom, a halogen atom, a nitro group, a carboxyl group, a substituted or unsubstituted alkyl group, or the like, and

R.sup.3 is a hydrogen atom, a substituted or unsubstituted alkyl group, or the like;

a prodrug of said compound, or a pharmaceutically acceptable salt of said compound or prodrug is a useful compound as a therapeutic agent for diseases for which Rho kinase is responsible.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AI 20020606
DETD [0336] Synthesis of N-(1-benzyl-4-piperidinyl)-1H-indazol-5-amine Dihydrochloride Monohydrate
DETD [0340] (b) Synthesis of N-(1-benzyl-4-piperidinyl)-1H-indazol-5-amine Dihydrochloride Monohydrate
DETD . . . at room temperature for 30 minutes. The solid precipitated was collected by filtration and recrystallized from methanol to obtain N-(1-benzyl-4-piperidinyl)-1H-indazol-5-amine dihydrochloride monohydrate (2.86 g, 72%).
DETD [0344] N-[1-(2-phenylethyl)-4-piperidinyl)]-1H-indazol-5-amine dihydrochloride
DETD [0362] N-cyclohexyl-1H-indazol-5-amine Monohydrochloride
DETD [0370] Synthesis of N-(4-piperidinyl)-1H-indazol-5-amine Dihydrochloride Monohydrate
DETD [0374] (b) Synthesis of N-(4-piperidinyl)-1H-indazol-5-amine Dihydrochloride Monohydrate
DETD . . . minutes. The solid precipitated was collected by filtration and

recrystallized from a mixture of chloroform and methanol to obtain N-(4-piperidinyl)-1H-indazol-5-amine dihydrochloride monohydrate (2.86 g, 72%).

DETD . . . solution of 5-aminoindazole (1.00 g, 7.51 mmol) in N,N-dimethylformamide (15 ml) were added 4-methylvaleric acid (960 mg, 8.26 mmol), 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide monohydrochloride (1.72 g, 9.01 mmol), hydroxybenzotriazole (1.12 g, 8.26 mmol) and triethylamine (1.7 ml, 12.0 mmol), and the resulting mixture was. . .

DETD . . . solution of 1H-indazole-5-carboxylic acid (400 mg, 2.47 mmol) in N,N-dimethylformamide (8 ml) were added 1-benzylpiperazine (435 mg 2.47 mmol), 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide monohydrochloride (565 mg, 2.96 mmol), hydroxybenzotriazole (367 mg, 2.72 mmol) and triethylamine (0.56 ml, 3.95 mmol), and the resulting mixture was. . .

DETD . . . To a solution of 1-(1H-indazol-5-yl)methanamine (291 mg) in N,N-dimethylformamide (8 ml) were added 1-(tert-butoxycarbonyl)-4-piperidinecarboxylic acid (507 mg, 2.21 mmol), 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide monohydrochloride (578 mg, 3.02 mmol) and hydroxybenzotriazole (229 mg, 2.21 mmol), and the resulting mixture was stirred at room temperature for. . .

DETD [0560] To a solution of 2-(1H-indazol-5-ylamino)benzoic acid (80 mg, 0.316 mmol) in N,N-dimethylformamide (0.5 ml) were added 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide monohydrochloride (73 mg, 0.379 mmol), hydroxybenzotriazole (58 mg, 0.379 mmol) and a 40%-aqueous dimethylamine solution (107 mg, 0.948 mmol), and the. . .

DETD [0567] N-(1-benzyl-4-piperidinyl)-1H-indazol-4-amine Dihydrochloride

DETD [0574] N-(4-piperidinyl)-1H-indazol-4-amine Dihydrochloride

DETD [0579] N-(1-benzyl-4-piperidinyl)-1H-indazol-6-amine Dihydrochloride

DETD [0584] N-(4-piperidinyl)-1H-indazol-6-amine Dihydrochloride

DETD [0592] N-(1-benzyl-4-piperidinyl)-1-methyl-1H-indazol-5-amine Dihydrochloride

DETD [0598] 1-Methyl-N-(4-piperidinyl)-1H-indazol-5-amine Dihydrochloride

DETD [0603] N-(1-benzyl-4-piperidinyl)-2-methyl-2H-indazol-5-amine Dihydrochloride

DETD [0608] 2-Methyl-N-(4-piperidinyl)-2H-indazol-5-amine Dihydrochloride

DETD [0615] N-(1-benzyl-4-piperidinyl)-3-methyl-1H-indazol-5-amine Dihydrochloride

DETD [0620] 3-Methyl-N-(4-piperidinyl)-1H-indazol-5-amine Dihydrochloride

DETD [0728] (d) Synthesis of 1-benzyl-3-piperidinamine Dihydrochloride

DETD . . . the residue to precipitate a solid, and the supernatant was decanted and then dried under reduced pressure to obtain 1-benzyl-3-piperidinamine dihydrochloride (0.384 g, 95%).

DETD . . . g, 1.39 mmol) obtained in Reference Example 1, triethylamine (0.57 ml, 4.1 mmol), 1-hydroxybenztriazole (0.222 g, 1.64 mmol) and 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide monohydrochloride (0.314 g, 1.64 mmol) were added to a solution of 1-benzyl-3-piperidinamine dihydrochloride (0.360 g, 1.37 mmol) in N,N-dimethylformamide (5 ml) and stirred overnight. The resulting mixture was added to a 1N-aqueous sodium. . .

DETD . . . Example 1 in N,N-dimethylformamide (15 ml) were added trans-tert-butyl 4-aminocyclohexylcarbamate (317 mg, 1.48 mmol), triethylamine (0.172 ml, 1.23 mmol), 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide monohydrochloride (355 mg, 1.85 mmol) and hydroxybenzotriazole (200 mg, 1.48 mmol), and the resulting mixture was stirred at room temperature for. . .

DETD [0915] A solution of dibenzylamine (0.448 g, 2.27 mmol) in dichloromethane (3 ml), 1-hydroxybenztriazole (0.337 g, 2.49 mmol) and 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide monohydrochloride (0.477 g, 2.49 mmol) were added to a solution of 3-[(tert-

butoxycarbonyl)amino]cyclohexanecarboxylic acid (0.502 g, 2.06 mmol) in dichloromethane (7 ml). . .

DETD [0916] (c) Synthesis of 3-amino-N,N-dibenzylcyclohexane-carboxamide Monohydrochloride

DETD . . . ml) and stirred overnight. The solvent was distilled off under reduced pressure, followed by replacement with toluene (twice), whereby 3-amino-N,N-dibenzylcyclohexanecarboxamide monohydrochloride (0.848 g, >99%) was obtained.

DETD [0919] A solution of 3-amino-N,N-dibenzylcyclohexane-carboxamide monohydrochloride (0.848 g) in tetrahydrofuran (5 ml) was added dropwise to a suspension of lithium aluminum hydride (0.337 g, 8.89 mmol). . .

DETD [0921] The 1H-indazole-5-carboxylic acid (0.285 g, 1.75 mmol) obtained in Reference Example 1, 1-hydroxybenztriazole (0.285 g, 2.11 mmol) and 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide monohydrochloride (0.409 g, 2.13 mmol) were added to a solution of 3-[(dibenzylamino)methyl]cyclohexanamine (0.542 g, 1.76 mmol) in N,N-dimethylformamide (5 ml) and. . .

DETD [0957] (c) Synthesis of 4-amino-1-benzyl-2-pyrrolidinone Hydrochloride

DETD . . . minutes and the precipitate was collected by filtration. The precipitate was washed with diethyl ether and dried to obtain 4-amino-1-benzyl-2-pyrrolidinone hydrochloride (380 mg, 99%).

DETD [0961] N-(1-benzyl-5-oxo-3-pyrrolidinyl)-1H-indazole-5-carboxamide was obtained by carrying out reaction according to the method described in Example 45, except for using 4-amino-1-benzyl-2-pyrrolidinone hydrochloride.

DETD [1049] Synthesis of N-(piperidin-4-ylmethyl)-1H-indazole-5-carboxamide Hydrochloride

DETD [1053] (b) Synthesis of N-(piperidin-4-ylmethyl)-1H-indazole-5-carboxamide Hydrochloride

DETD . . . 1 hour with heating under reflux while maintaining the temperature. The resulting mixture was concentrated to dryness to obtain N-(piperidin-4-ylmethyl)-1H-indazole-5-carboxamide hydrochloride (29.8 mg, 100%).

DETD . . . Reference Example 1 in N,N-dimethylformamide (10 ml) were added 1-benzyl-N-methylpiperidin-4-amine (390 mg, 1.91 mmol), triethylamine (0.29 ml, 2.08 mmol), 1-ethyl-3-(3'-dimethylaminopropyl)-carbodiimide monohydrochloride (499 mg, 2.60 mmol) and hydroxybenzotriazole (281 mg, 2.08 mmol), and the resulting mixture was stirred overnight at room temperature.. . .

DETD [1257] Potassium carbonate (1.64 g, 11.9 mmol) and N-carboethoxyphthalimide (1.59 g, 7.25 mmol) were added to a solution of 4-aminocyclohexanol hydrochloride (1.0 g, 6.59 mmol) in water (15 ml) at room temperature and stirred for 30 minutes. The reaction solution was. . .

DETD [1289] Synthesis of trans-3-(1H-indazol-4-yloxy)-cyclohexanamine Hydrochloride

DETD . . . was crystallized by the addition of acetonitrile, followed by filtration. The precipitate was dried under reduced pressure to obtain trans-3-(1H-indazol-4-yloxy)-cyclohexanamine hydrochloride (166 mg, 88%).

DETD [1303] Synthesis of 5-(piperidin-4-ylmethoxy)-1H-indazole dihydrochloride

DETD [1308] (c) Synthesis of 5-(piperidin-4-ylmethoxy)-1H-indazole Dihydrochloride

DETD . . . and crystallized from diethyl ether (10 ml). The crystals were filtered and then dried under reduced pressure to obtain 5-(piperidin-4-ylmethoxy)-1H-indazole dihydrochloride (71 mg, 95%).

DETD . . . obtained in Example 368 in N,N-dimethylformamide (10 ml). After aqueous ammonia (1 ml) was added thereto to effect dissolution,

1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide monohydrochloride (309 mg, 1.61 mmol) and hydroxybenzotriazole (160 mg, 1.18 mmol) were added thereto. After 16 hours, it was confirmed that the starting material remained. Therefore, 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide monohydrochloride (309 mg, 1.61 mmol) and hydroxybenzotriazole (160 mg, 1.18 mmol) were further added thereto. After 7 hours, a saturated aqueous. . .

DETD [1465] Synthesis of trans-4-(1H-indazol-5-yloxy)-N,N-dimethylcyclohexanamine Monohydrochloride

DETD . . . ml). The solid precipitated was subjected to decantation with ethyl acetate (three times) and then dried up to obtain trans-4-(1H-indazol-5-yloxy)-N,N-dimethylcyclohexanamine monohydrochloride (0.0400 g, 86%).

DETD [1469] trans-4-(1H-indazol-5-yloxy)-N-propylcyclo-hexanamine Monohydrochloride

DETD [1472] Acetic acid (0.033 g, 0.58 mmol), triethylamine (0.12 ml, 0.86 mmol), 1-hydroxybenztriazole (0.088 g, 0.65 mmol) and 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide monohydrochloride (0.124 g, 0.65 mmol) were added to a solution of the trans-4-(1H-indazol-5-yloxy)cyclohexanamine (0.100 g, 0.44 mmol) obtained in Example 384. . .

DETD [1474] Synthesis of trans-N-ethyl-4-(1H-indazol-5-yloxy)cyclohexanamine Monohydrochloride

DETD . . . ml) was added thereto. The solid precipitated was subjected to decantation with ethyl acetate and dried up to obtain trans-N-ethyl-4-(1H-indazol-5-yloxy)cyclohexanamine monohydrochloride (0.057 g, 80%).

DETD [1494] Synthesis of trans-N,N-diethyl-3-(1H-indazol-5-yloxy)cyclohexanamine monohydrochloride

DETD [1497] (b) Synthesis of trans-N,N-diethyl-3-(1H-indazol-5-yloxy)cyclohexanamine Monohydrochloride

DETD [1498] Except for using trans-N-ethyl-N-[3-(1H-indazol-5-yloxy)cyclohexyl]acetamide, trans-N,N-diethyl-3-(1H-indazol-5-yloxy)cyclohexanamine monohydrochloride was obtained by carrying out reaction according to the method described in Example 392.

DETD [1536] cis-4-[(4-Methyl-1H-indazol-5-yl)oxy]cyclo-hexanamine hydrochloride

DETD [1551] trans-N-butyl-4-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexanamine monohydrochloride

DETD [1569] trans-N,N-diethyl-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexanamine Monohydrochloride

DETD . . . and the resulting mixture was stirred at room temperature for 1 hour. The solvent was distilled off, and to the hydrochloride thus obtained was added a 1N-aqueous sodium hydroxide solution (100 ml), followed by extraction with ethyl acetate (60 ml) (twice).. . .

DETD . . . a mixture of the 4-methyl-5-(piperidin-3-yloxy)-1H-indazole (92 mg, 0.40 mmol) obtained in Example 422, acetic acid (24 mg, 0.40 mmol), 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide monohydrochloride (77 mg, 0.40 mmol), 1-hydroxybenzo-triazole (54 mg, 0.40 mmol) and N,N-dimethylformamide (1.5 ml), and the resulting mixture was stirred at. . .

DETD . . . 0.317 mmol) synthesized in Example 479 and isobutylamine (301 mg, 0.412 mmol) were dissolved in N,N-dimethylformamide (2 ml), and dimethylamine hydrochloride (72.5 mg, 0.380 mmol), hydroxybenzotriazole (47.1 mg, 0.349 mmol) and triethylamine (0.09 ml, 0.634 mmol) were added thereto at room. . .

DETD [1770] The 2-(1H-indazol-5-yloxy)benzoic acid (80.8 mg, 0.318 mmol) synthesized in Example 479 and dimethylamine hydrochloride (33.7 mg, 0.413 mmol) were dissolved in N,N-dimethylformamide (2 ml), and 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide monohydrochloride (72.5

mg, 0.380 mmol), hydroxybenzotriazole (47.1 mg, 0.349 mmol) and triethylamine (0.13 ml, 0.954 mmol) were added thereto at room. . .

DETD [1781] Synthesis of 1-[2-(1H-indazol-5-yloxy)phenyl]-N,N-dimethylmethanamine Monohydrochloride

DETD [1785] (b) Synthesis of 1-[2-(1H-indazol-5-yloxy)phenyl]-N,N-dimethylmethanamine Monohydrochloride

DETD . . . acid/diethyl ether solution (0.3 ml) was added dropwise thereto at 0° C. The resulting suspension was concentrated to obtain 1-[2-(1H-indazol-5-yloxy)phenyl]-N,N-dimethylmethanamine monohydrochloride (20 mg).

DETD [1788] Synthesis of N-[2-(1H-indazol-5-yloxy)benzyl]-2-methylpropan-1-amine Monohydrochloride

DETD [1789] N-[2-(1H-indazol-5-yloxy)benzyl]-2-methylpropan-1-amine monohydrochloride was synthesized by carrying out reaction according to the method described in Example 484, except for using the 2-(1H-indazol-5-yloxy)-N-isobutylbenzamide obtained. . .

DETD [1842] Tetrahydro-2H-pyran-4-ylamine monohydrochloride (228 mg, 1.66 mmol), triethylamine (0.5 ml, 3.59 mmol), 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide monohydrochloride (367 mg, 1.91 mmol) and hydroxybenzotriazole (190 mg, 1.41 mmol) were added to a solution of 4-methyl-1H-indazole-5-carboxylic acid (225 mg,. . .

DETD [1857] (d) Synthesis of Methyl 4-amino-2,5-dimethylbenzoate Monohydrochloride

DETD [1860] Triethylamine (1.16 ml, 8.32 mmol) was added to a suspension of methyl 4-amino-2,5-dimethylbenzoate monohydrochloride (0.600 g, 2.78 mmol) in dichloromethane (8 ml), and the resulting mixture was cooled with ice water, followed by adding. . .

DETD [1866] Tetrahydro-2H-pyran-4-ylamine monohydrochloride (0.0402 g, 0.292 mmol), triethylamine (0.07 ml, 0.5 mmol), 1-hydroxybenztriazole (0.0460 g, 0.340 mmol) and 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide monohydrochloride (0.0606 g, 0.316 mmol) were added to a solution of 6-methyl-1H-indazole-5-carboxylic acid (0.0437 g, 0.248 mmol) in N,N-dimethylformamide (2 ml). . .

DETD [1928] A 28%-aqueous ammonia solution (57.6 mg, 0.948 mmol), 1-hydroxybenzotriazole (58 mg, 0.379 mmol) and 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (73 mg, 0.379 mmol) were added in that order to a solution of 2-(1H-indazol-5-ylamino)benzoic acid (80.0 mg, 0.316 mmol) in. . .

DETD . . . 0.402 mmol) in N,N-dimethylformamide (0.5 ml) were added 1-benzylpiperazine (210 μl, 1.21 mmol), 1-hydroxybenzotriazole (74 mg, 0.484 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (94 mg, 0.490 mmol) in that order, and the resulting mixture was stirred at room temperature for 21 hours. The. . .

DETD [2088] Hydroxyacetic acid (32 mg, 0.421 mmol), 1-hydroxybenzotriazole (76 mg, 0.496 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (95 mg, 0.496 mmol) were added in that order to a suspension of the N-(8-azabicyclo[3.2.1]oct-3-yl)-1H-indazol-5-amine (100 mg, 0.413 mmol) obtained. . .

DETD [2095] Synthesis of N-(1-azabicyclo[2.2.2]oct-3-yl)-1H-indazol-5-amine Dihydrochloride

DETD . . . was added thereto, the solid formed was collected by filtration, washed with diethyl ether and then dried to obtain N-(1-azabicyclo[2.2.2]oct-3-yl)-1H-indazol-5-amine dihydrochloride (210 mg, 91%).

DETD [2099] 2-[3-(1H-indazol-5-ylamino)-8-azabicyclo[3.2.1]oct-8-yl]ethanol Dihydrochloride

DETD [2102] N-(8-propyl-8-azabicyclo[3.2.1]oct-3-yl)-1H-indazol-5-amine dihydrochloride

DETD [2107] 4-Methoxy-5-(4-piperidinyloxy)-1H-indazole Monohydrochloride

DETD [2110] 4-Methoxy-5-(3-piperidinyloxy)-1H-indazole Monohydrochloride

DETD [2118] trans-4-[(4-Methoxy-1H-indazol-5-yl)oxy]cyclohexanamine monohydrochloride

DETD [2120] cis-4-[(4-Methoxy-1H-indazol-5-yl)oxy]cyclo-hexanamine Monohydrochloride

DETD [2144] (a) Synthesis of cis-3-amino-4,4-dimethylcyclohexanol Hydrochloride

DETD . . . removed by filtration using Celite, the filtrate was concentrated under reduced pressure and the resulting residue was converted to its hydrochloride with a 1N-HCl ether solution to obtain cis-3-amino-4,4-dimethylcyclohexanol hydrochloride (720 mg, 95%, containing about 15% of trans isomer) as white powder.

DETD . . . ml), potassium carbonate (3.1 mmol, 423 mg) and N-carboethoxyphthalimide (3.1 mmol, 670 mg) were added to a solution of cis-3-amino-4,4-dimethylcyclohexanol hydrochloride (500 mg, 2.8 mmol) in water (10 ml), and the resulting mixture was stirred as it was for 2 hours.. . .

DETD [2170] Synthesis of 1-{4-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}-methanamine hydrochloride

DETD [2184] (g) Synthesis of 1-{4-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}-methanamine Hydrochloride

DETD . . . off under reduced pressure, and the residue was solidified with isopropyl alcohol-diisopropyl ether, filtered and then dried to obtain 1-{4-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}-methanamine hydrochloride (148 mg, 87%).

DETD [2187] Synthesis of cis-4-[(4-chloro-1H-indazol-5-yl)oxy]cyclohexanamine hydrochloride

DETD [2190] (b) Synthesis of cis-4-[(4-chloro-1H-indazol-5-yl)oxy]cyclohexanamine Hydrochloride

DETD . . . to the reaction suspension and the resulting mixture was filtered. Then, the precipitate was dried under pressure to obtain cis-4-[(4-chloro-1H-indazol-5-yl)oxy]cyclohexanamine hydrochloride (57.8 mg, 94%).

DETD [2199] Synthesis of 5-(piperidin-4-yloxy)-4-chloro-1H-indazole Hydrochloride

DETD . . . obtained was concentrated under reduced pressure and the resulting residue was washed with ethyl acetate by repulping to obtain 5-(piperidin-4-yloxy)-4-chloro-1H-indazole hydrochloride (219.7 mg, 86%).

DETD [2246] Synthesis of 5-(azepan-4-yloxy)-4-(methylthio)-1H-indazole monohydrochloride

DETD [2251] (c) Synthesis of 5-(azepan-4-yloxy)-4-(methylthio)-1H-indazole Monohydrochloride

DETD [2254] Synthesis of 5-(azepan-4-yloxy)-4-(methylsulfonyl)-1H-indazole monohydrochloride

DETD [2257] (b) Synthesis of 5-(azepan-4-yloxy)-4-(methylsulfonyl)-1H-indazole Monohydrochloride

DETD [2263] Synthesis of cis-4-{[4-(methylthio)-1H-indazol-5-yl]oxy}cyclohexanamine monohydrochloride

DETD [2266] (b) Synthesis of cis-4-{[4-(methylthio)-1H-indazol-5-yl]oxy}cyclohexanamine Monohydrochloride

DETD [2307] Synthesis of cis-4-{[4-(methylthio)-1H-indazol-5-yl]oxy}-N-propylcyclohexanamine Monohydrochloride

DETD [2310] (b) Synthesis of cis-4-{[4-(methylthio)-1H-indazol-5-yl]oxy}-N-propylcyclohexanamine Monohydrochloride

DETD [2313] Synthesis of cis-N-benzyl-4-{[4-(methylthio)-1H-indazol-5-yl]oxy}cyclohexanamine monohydrochloride

DETD [2316] (b) Synthesis of cis-N-benzyl-4-{[4-(methylthio)-1H-indazol-5-yl]oxy}cyclohexanamine Monohydrochloride

DETD [2340] Synthesis of cis-4-{[4-(ethylthio)-1H-indazol-5-yl]oxy}cyclohexanamine Monohydrochloride

DETD [2343] (b) Synthesis of cis-4-{[4-(ethylthio)-1H-indazol-5-yl]oxy}cyclohexanamine Monohydrochloride

DETD [2374] Synthesis of cis-3-[(4-propoxy-1H-indazol-5-yl)oxy]cyclohexanamine Hydrochloride

DETD [2377] (b) Synthesis of cis-3-[(4-propoxy-1H-indazol-5-yl)oxy]cyclohexanamine Hydrochloride

DETD . . . filtration under reduced pressure, and then drying. The solid thus obtained was washed with hexane by repulping to obtain cis-3-[(4-propoxy-1H-indazol-5-yl)oxy]cyclohexanamine hydrochloride (76.8 mg, 83%).

DETD [2381] Synthesis of cis-4-[(4-propoxy-1H-indazol-5-yl)oxy]cyclohexanamine Hydrochloride

DETD . . . Under a nitrogen atmosphere, triethylamine (49.5 μl, 0.355 mmol) was added at 0° C. to a solution of the cis-4-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexanamine hydrochloride (100 mg, 0.355 mmol) obtained in Example 410 in tetrahydrofuran (4 ml), followed by adding dropwise thereto a solution of. . .

DETD [2389] Synthesis of cis-3-[(4-isopropoxy-1H-indazol-5-yl)oxy]cyclohexanamine hydrochloride

DETD [2392] (b) Synthesis of cis-3-[(4-isopropoxy-1H-indazol-5-yl)oxy]cyclohexanamine Hydrochloride

DETD . . . filtration under reduced pressure, and then drying. The solid thus obtained was washed with hexane by repulping to obtain cis-3-[(4-isopropoxy-1H-indazol-5-yl)oxy]cyclo-hexanamine hydrochloride (70.1 mg, 74%).

DETD [2396] cis-4-[(4-Isopropoxy-1H-indazol-5-yl)oxy]cyclohexanamine Hydrochloride

DETD . . . succinic anhydride (105 mg, 1.05 mmol) and triethylamine (279 μl, 2.00 mmol) were added to a solution of the cis-4-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexanamine hydrochloride (282 mg, 1.00 mmol) obtained in Example 410 in toluene (6 ml) at room temperature, and the resulting mixture was. . .

DETD . . . 15 minutes at room temperature. After 40 minutes, the solution thus prepared was slowly dropped into a solution of cis-2-aminocyclohexanol hydrochloride (1.0 g, 6.65 mmol) and triethylamine (1.01 ml, 7.31 mmol) in tetrahydrofuran (10 ml). After 3 hours, p-toluenesulfonic acid (35. . .

DETD [2427] Synthesis of {trans-2-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}methylamine hydrochloride

DETD . . . (375 mg, 2.72 mmol) and ethoxycarbonylphthalimide (364 mg, 1.66 mmol) were added to an aqueous solution (4 ml) of 2-aminomethylcyclohexanol hydrochloride (250 mg, 1.51 mmol) at room temperature. After 3 hours, the reaction solution was poured into water and extracted with. . .

DETD [2432] (c). Synthesis of {trans-2-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}methylamine Hydrochloride

DETD . . . hour, the reaction solution was concentrated under reduced pressure and the resulting residue was crystallized from 2-propanol/acetonitrile to obtain {trans-2-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}methylamine hydrochloride (49.4 mg, 81%).

DETD [2443] Synthesis of {cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}methylamine Hydrochloride

DETD [2452] (e) Synthesis of {cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}methylamine Hydrochloride

DETD . . . the reaction solution was concentrated under reduced pressure and the resulting residue was crystallized from 2-propanol/diethyl ether to obtain {cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}methylamine hydrochloride (21.8 mg, 74%).

DETD . . . nitrogen atmosphere, triethylamine (112 μl, 0.807 mmol) and

acetyl chloride (25.2 μl, 0.355 mmol) were added to a solution of monohydrochloride (100 mg, 0.323 mmol) of the trans-N,N-dimethyl-N-{4-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}amine obtained in Example 412 in N,N-dimethylformamide (2 ml) at room temperature. After 1. . .

DETD . . . (135 μl, 0.968 mmol) and methyl chloroformate (37 μl, 0.484 mmol) were added at 0° C. to a solution of monohydrochloride (100 mg, 0.323 mmol) of the trans-N,N-dimethyl-N-{4-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}amine obtained in Example 412 in acetone (2 ml). After 15 minutes, the mixture. . .

DETD [2543] Triethylamine (108 μl, 0.775 mmol), propionic acid (32 μl, 0.429 mmol), 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (83 mg, 0.433 mmol) and 1-hydroxybenzotriazole (58 mg, 0.429 mmol) were added in that order to a dimethylformamide solution (2. . .

DETD [2647] Synthesis of N-[cis-3-[(4-methoxy-1H-indazol-5-yl)oxy]cyclohexyl]-N,N-dimethylamine Monohydrochloride

DETD . . . 4N-hydrochloric acid/dioxane solution was added thereto and stirred. Then, the solvent was distilled off under reduced pressure to obtain N-[cis-3-[(4-methoxy-1H-indazol-5-yl)oxy]cyclohexyl]-N,N-dimethylamine monohydrochloride (43 mg, yield 34%).

DETD [2650] Synthesis of N-ethyl-N-[cis-3-[(4-methoxy-1H-indazol-5-yl)oxy]cyclohexyl]amine Monohydrochloride

DETD . . . acetic acid (25 μl, 0.421 mmol) and triethylamine (107 μl, 0.765 mmol) were added thereto, followed by adding thereto 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide mono-hydrochloride (81 mg, 0.421 mmol) and 1-hydroxybenzotriazole (57 mg, 0.421 mmol). The resulting mixture was stirred at room temperature for 21. . .

DETD [2654] (b) Synthesis of N-ethyl-N-[cis-3-[(4-methoxy-1H-indazol-5-yl)oxy]cyclohexyl]amine Monohydrochloride

DETD . . . alcohol, followed by adding thereto a 4N-hydrochloric acid/dioxane solution, and the resulting mixture was concentrated to dryness to obtain N-ethyl-N-[cis-3-[(4-methoxy-1H-indazol-5-yl)oxy]cyclohexyl]amine monohydrochloride (40 mg, yield 35%).

DETD . . . propionic acid (31 μl, 0.421 mmol) and triethylamine (107 μl, 0.765 mmol) were added thereto, followed by adding thereto 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide mono-hydrochloride (81 mg, 0.421 mmol) and 1-hydroxybenzotriazole (57 mg, 0.421 mmol). The resulting mixture was stirred at room temperature for 24. . .

DETD . . . carrying out reaction according to the method described in Example 700, except for using a free form of the cis-4-[(4-methoxy-1H-indazol-5-yl)oxy]cyclohexanamine monohydrochloride obtained in Example 585, as a starting material.

DETD [2725] Synthesis of 4-methyl-5-[(cis-3-pyrrolidin-1-ylcyclohexyl)oxy]-1H-indazole Monohydrochloride

DETD . . . Then, a 4N-hydrochloric acid/1,4-dioxane solution was added thereto and the solvent was distilled off under reduced pressure to obtain 4-methyl-5-[(cis-3-pyrrolidin-1-ylcyclohexyl)oxy]-1H-indazole monohydrochloride (55 mg, yield 100%) as a hygroscopic light-yellow solid.

DETD [2741] Synthesis of N-[cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl]-N-phenylamine monohydrochloride

DETD [2744] (b) Synthesis of N-[cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl]-N-phenylamine Monohydrochloride

DETD [2761] Synthesis of 4-[(4-methyl-1H-indazol-5-yl)oxy]aniline Monohydrochloride

DETD . . . washed with the filtrate and then a small volume of isopropyl alcohol, and dried under reduced pressure to obtain 4-[(4-methyl-1H-indazol-5-yl)oxy]aniline monohydrochloride (39 mg, yield 78%) as a white solid.

DETD [2770] Synthesis of 3-[(4-methyl-1H-indazol-5-yl)oxy]aniline Monohydrochloride

DETD . . . The white solid precipitated was collected by filtration, washed with diethyl ether, and dried under reduced pressure to obtain 3-[(4-methyl-1H-indazol-5-yl)oxy]aniline monohydrochloride (50 mg, yield 81%) as a white solid.

DETD [2776] Synthesis of 3-chloro-4-[(4-methyl-1H-indazol-5-yl)oxy]aniline Monohydrochloride

DETD . . . yellow solid precipitated was collected by filtration, washed with diethyl ether and then dried under reduced pressure to obtain 3-chloro-4-[(4-methyl-1H-indazol-5-yl)oxy]aniline monohydrochloride (45 mg, yield 42%).

DETD [2779] Synthesis of 3-[(4-methyl-1H-indazol-5-yl)oxy]benzonitrile Monohydrochloride

DETD [2782] (b) Synthesis of 3-[(4-methyl-1H-indazol-5-yl)oxy]benzonitrile Monohydrochloride

DETD . . . stirred, the precipitate was collected by filtration, washed with diethyl ether and then dried under reduced pressure to obtain 3-[(4-methyl-1H-indazol-5-yl)oxy]benzonitrile hydrochloride (176 mg, yield 69%).

DETD [2785] Synthesis of 4-[(4-methyl-1H-indazol-5-yl)oxy]benzonitrile Monohydrochloride

DETD [2788] (b) Synthesis of 4-[(4-methyl-1H-indazol-5-yl)oxy]benzonitrile Monohydrochloride

DETD . . . stirred, the precipitate was collected by filtration, washed with diethyl ether and then dried under reduced pressure to obtain 4-[(4-methyl-1H-indazol-5-yl)oxy]benzonitrile monohydrochloride (239 mg, yield 83%).

DETD [2791] Synthesis of 1-[4-[(4-methyl-1H-indazol-5-yl)oxy]phenyl]methylamine Monohydrochloride

DETD [2792] Under nitrogen, the 4-[(4-methyl-1H-indazol-5-yl)oxy]benzonitrile monohydrochloride (70 mg, 0.245 mmol) obtained in Example 741 was suspended in tetrahydrofuran (2 ml), and lithium aluminum hydride (46 mg,. . . resulting white solid was collected by filtration, washed with diethyl ether and then dried under reduced pressure to obtain 1-[4-[(4-methyl-1H-indazol-5-yl)oxy]phenyl]methylamine monohydrochloride (46 mg, yield 65%).

DETD [2794] Synthesis of 1-[3-[(4-methyl-1H-indazol-5-yl)oxy]phenyl]methylamine Monohydrochloride

DETD [2795] Under nitrogen, the 3-[(4-methyl-1H-indazol-5-yl)oxy]benzonitrile monohydrochloride (60 mg, 0.210 mmol) obtained in Example 740 was suspended in tetrahydrofuran (2 ml), and lithium aluminum hydride (40 mg,. . . resulting white solid was collected by filtration, washed with diethyl ether and then dried under reduced pressure to obtain 1-[3-[(4-methyl-1H-indazol-5-yl)oxy]phenyl]methylamine monohydrochloride (39 mg, yield 64%).

DETD [2800] (b) 4-((4-Ethyl-1H-indazol-5-yl)oxy)cyclohexanamine hydrochloride was obtained by carrying out reaction according to the method described in Example 14, except for using trans-2-{4-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}-1H-isoindole-1,3(2H)-dione.

DETD [2812] trans-N,N-dimethyl-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexanamine monohydrochloride

DETD [2814] trans-N,N-dipropyl-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexanamine monohydrochloride

DETD [2825] Synthesis of trans-N-propyl-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexanamine Monohydrochloride

DETD [2828] (b) Synthesis of trans-N-propyl-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexanamine Monohydrochloride

DETD [2845] Acetic acid (0.036 g, 0.60 mmol), triethylamine (0.21 ml, 1.5 mmol), 1-hydroxybenztriazole (0.081 g, 0.60 mmol) and

1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide monohydrochloride (0.115 g, 0.60 mmol) were added to a solution of the cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexylamine (147 mg, 0.60 mmol) obtained in Example 411. . .

DETD [2855] Acetic acid (0.013 g, 0.22 mmol), triethylamine (0.070 ml, 0.50 mmol), 1-hydroxybenztriazole (0.029 g, 0.22 mmol) and 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide monohydrochloride (0.042 g, 0.22 mmol) were added to a solution of the N-ethyl-N-cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexylamine (59.4 mg, 0.217 mmol) obtained in Example 758. . .

DETD [2870] Acetic acid (0.014 g, 0.22 mmol), triethylamine (0.075 ml, 0.54 mmol), 1-hydroxybenztriazole (0.030 g, 0.22 mmol) and 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide monohydrochloride (0.043 g, 0.22 mmol) were added to a solution of the cis-3-[(4-trifluoromethyl-1H-indazol-5-yl)oxy]cyclohexylamine (0.066 g, 0.22 mmol) obtained in Example 587. . .

DETD [2916] Cyclopropanecarboxylic acid (0.034 g, 0.40 mmol), triethylamine (0.14 ml, 1.0 mmol), 1-hydroxybenztriazole (0.054 g, 0.40 mmol) and 1-ethyl-3-(3'-dimethylamino-propyl)carbodiimide monohydrochloride (0.077 g, 0.40 mmol) were added to a solution of the trans-4-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexylamine (98 mg, 0.40 mmol) obtained in Example 408. . .

DETD [3026] Synthesis of 4-methyl-5-[(4-morpholin-cis-4-ylcyclohexyl)oxy]-1H-indazole hydrochloride

DETD [3033] (d) Synthesis of 4-methyl-5-[(4-morpholin-cis-4-ylcyclohexyl)oxy]-1H-indazole Hydrochloride

DETD . . . maintaining at room temperature. The white precipitate formed was collected by filtration and dried under reduced pressure to obtain 4-methyl-5-[(4-morpholin-cis-4-ylcyclohexyl)oxy]-1H-indazole hydrochloride (149 mg, 91%).

DETD [3042] Isobutyric acid (36.2 μL, 0.39 mmol), 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide monohydrochloride (74.8 mg, 0.39 mmol), hydroxybenzotriazole (52.8 mg, 0.39 mmol) and triethylamine (0.18 ml, 1.28 mmol) were added to a solution of monohydrochloride (100 mg, 0.35 mmol) of the cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexanamine obtained in Example 411 in N,N-dimethylformamide (5 ml), and the resulting mixture was. . .

DETD [3059] Synthesis of N-isobutyl-N-{cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}amine Monohydrochloride

DETD . . . the solvent was distilled off under reduced pressure. Then, the residue was crystallized from 2-propanol-diisopropyl ether-diethyl ether to obtain N-isobutyl-N-{cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}amine monohydrochloride (42.0 mg, 49%).

DETD [3062] Synthesis of N-{cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}-N-(tetrahydrofuran-3-ylmethyl)amine Monohydrochloride

DETD [3063] N-{cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}-N-(tetrahydrofuran-3-ylmethyl)amine monohydrochloride was obtained according to the process described in Example 827, except for using the N-{cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}tetrahydrofuran-3-carboxamide obtained in Example 820.

DETD [3065] Synthesis of N-(2-methoxyethyl)-N-{cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}amine Monohydrochloride

DETD [3066] N-(2-methoxyethyl)-N-{cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}amine monohydrochloride was obtained according to the process described in Example 827, except for using the 2-methoxy-N-{cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}acetamide obtained in Example 821.

DETD [3068] Synthesis of N-(cyclopropylmethyl)-N-{cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}amine Monohydrochloride

DETD [3069] N-(cyclopropylmethyl)-N-{cis-3-[(4-methyl-1H-indazol-5-

yl)oxy]cyclohexyl}amine monohydrochloride was obtained according to the process described in Example 827, except for using the N-{cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}cyclopropanecarboxamide obtained in Example 823.

DETD [3071] Synthesis of N-{cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}-N-neopentylamine Monohydrochloride

DETD [3072] N-(3,3-dimethylbutyl)-N-{cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}amine monohydrochloride was obtained according to the process described in Example 827, except for using the 2,2-dimethyl-N-{cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}propanamide obtained in Example 824.

DETD [3074] Synthesis of N.about.1.about.-{cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}glycinamide Monohydrochloride

DETD . . . solvent was distilled off under reduced pressure, the residue was crystallized from 2-propanol-diisopropyl ether-diethyl ether to obtain N.about.1.about.(identification is required)-{cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}glycinamide monohydrochloride (39 mg, 79%).

DETD [3081] N-{cis-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}-N-(pyridin-3-ylmethyl)amine Monohydrochloride

DETD [3102] Synthesis of N-{cis-3-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}-N,N-dimethylamine monohydrochloride

DETD . . . solvent was distilled off under reduced pressure and then the residue was crystallized from 2-propanol-diisopropyl ether-diethyl ether to obtain N-{cis-3-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}-N,N-dimethylamine monohydrochloride (85.2 mg, 46%).

DETD [3105] Synthesis of cis-N-{4-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}-N,N-dimethylamine monohydrochloride

DETD [3106] Except for using the cis-4-((4-ethyl-1H-indazol-5-yl)oxy)cyclohexanamine obtained in Example 746, cis-N-{4-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}-N,N-dimethylamine monohydrochloride was obtained according to the process described in Example 842.

DETD [3108] Synthesis of N-{trans-3-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}-N,N-dimethylamine Monohydrochloride

DETD [3109] N-{trans-3-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}-N,N-dimethylamine monohydrochloride was obtained according to the process described in Example 842, except for using trans-3-((4-methyl-1H-indazol-5-yl)oxy)cyclohexanamine.

DETD [3126] Synthesis of trans-N-ethyl-4-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexanamine Monohydrochloride

DETD [3127] Except for using the trans-N-{4-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}acetamide obtained in Example 845, trans-N-ethyl-4-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexanamine monohydrochloride was obtained according to the process described in Example 827.

DETD [3129] Synthesis of trans-4-[(4-ethyl-1H-indazol-5-yl)oxy]-N-propylcyclohexanamine monohydrochloride

DETD [3132] (b) Synthesis of trans-4-[(4-ethyl-1H-indazol-5-yl)oxy]-N-propylcyclohexanamine Monohydrochloride

DETD [3133] Except for using trans-N-{4-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}propanamide, trans-4-[(4-ethyl-1H-indazol-5-yl)oxy]-N-propylcyclohexanamine monohydrochloride was obtained according to the process described in Example 827.

DETD [3135] Synthesis of N-ethyl-N-{cis-3-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}amine Monohydrochloride

DETD [3136] N-ethyl-N-{cis-3-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}amine monohydrochloride was obtained according to the process described in Example 827, except for using the N-{cis-3-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}acetamide obtained in Example 847.

DETD [3138] Synthesis of N-{cis-3-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}-N-propylamine Monohydrochloride

DETD [3141] (b) Synthesis of N-{cis-3-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}-N-propylamine Monohydrochloride

DETD [3142] N-{cis-3-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}-N-propylamine monohydrochloride was obtained by carrying out reaction according to the method described in Example 827, except for using N-{cis-3-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}propanamide.

DETD [3144] Synthesis of cis-N-ethyl-N-{4-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}amine Monohydrochloride

DETD [3145] Except for using the cis-N-{4-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}acetamide obtained in Example 848, cis-N-ethyl-N-{4-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}amine monohydrochloride was obtained according to the process described in Example 827.

DETD [3147] Synthesis of cis-N-{4-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}-N-propylamine Monohydrochloride

DETD [3148] Except for using the cis-4-((4-ethyl-1H-indazol-5-yl)oxy)cyclohexanamine obtained in Example 746, cis-N-{4-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}-N-propylamine monohydrochloride was obtained according to the process described in Example 853.

DETD [3150] Synthesis of N-ethyl-N-{trans-3-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}amine Monohydrochloride

DETD [3151] N-ethyl-N-{trans-3-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}amine monohydrochloride was obtained according to the process described in Example 827, except for using the N-{trans-3-[(4-methyl-1H-indazol-5-yl)oxy]cyclohexyl}acetamide obtained in Example 849.

DETD [3153] Synthesis of N-{trans-3-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}-N-propylamine Monohydrochloride

DETD [3154] N-{trans-3-[(4-ethyl-1H-indazol-5-yl)oxy]cyclohexyl}-N-propylamine monohydrochloride was obtained according to the process described in Example 853, except for using the trans-3-((4-ethyl-1H-indazol-5-yl)oxy)cyclohexanamine obtained in Example 747.

DETD [3156] Synthesis of 5-{(2S*4R*6S*)-[(2,6-dimethylpiperidin-4-yl)oxy]}-4-methyl-1H-indazole Hydrochloride

DETD [3158] Triethylamine (1.67 ml, 12.0 mmol) and di-tert-butyl dicarbonate (2.76 ml, 12.0 mmol) were added to a solution of (2S*4S*6S*)-2,6-dimethyl-4-hydroxypiperidine hydrochloride (388 mg, 3.00 mmol) in dimethylformamide (6 ml), and the resulting mixture was stirred at 60° C. for 3 hours.. . .

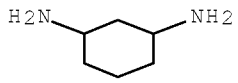
DETD [3159] (b) Synthesis of 5-{(2S*4R*6S*)-[(2,6-dimethylpiperidin-4-yl)oxy]}-4-methyl-1H-indazole Hydrochloride

DETD . . . temperature for 1 hour. After the solvent was distilled off, the residue was crystallized from methanol-ethyl acetate to obtain 5-{(2S*4R*6S*)-[(2,6-dimethylpiperidin-4-yl)oxy]}-4-methyl-1H-indazole hydrochloride (30 mg, 16%).

IT 50-00-0, Formalin, reactions 62-23-7, p-Nitrobenzoic acid 64-19-7, Acetic acid, reactions 67-64-1, Acetone, reactions 70-54-2, Lysine 74-88-4, Methyl iodide, reactions 74-89-5, Methylamine, reactions 75-36-5, Acetyl chloride 75-65-0, tert-Butanol, reactions 76-83-5, Triphenylmethyl chloride 78-81-9, Isobutylamine 79-04-9, Chloroacetyl chloride 79-09-4, Propionic acid, reactions 79-14-1, Hydroxyacetic acid, reactions 79-22-1, Methyl chloroformate 79-31-2, Isobutyric acid 80-62-6, Methyl methacrylate 85-41-6, Phthalimide 89-98-5, 2-Chlorobenzaldehyde 95-23-8 96-33-3, Methyl acrylate 96-41-3, Cyclopentanol 99-65-0, m-Dinitrobenzene 100-39-0, Benzyl bromide 100-44-7, Benzyl chloride, reactions 100-46-9, N-Benzylamine, reactions 100-52-7, Benzaldehyde, reactions 102-50-1, 4-Methoxy-2-methylaniline 103-49-1, Dibenzylamine 103-63-9, Phenethyl bromide 103-67-3, N-Benzylmethylamine 105-39-5, Chloroacetic acid ethyl ester 106-94-5, n-Propyl bromide 107-08-4, Propyl iodide 107-30-2, Chloromethyl methyl ether 108-24-7, Acetic anhydride 108-30-5, Succinic anhydride,

reactions 108-68-9, 3,5-Dimethylphenol 108-86-1, Bromobenzene, reactions 108-93-0, Cyclohexanol, reactions 110-52-1, 1,4-Dibromobutane 110-87-2, 3,4-Dihydro-2H-pyran 110-91-8, Morpholine, reactions 111-30-8, Glutaraldehyde 119-36-8, Salicylic acid methyl ester 123-38-6, Propionaldehyde, reactions 124-40-3, Dimethylamine, reactions 124-63-0, Methanesulfonyl chloride 143-33-9, Sodium cyanide 151-50-8, Potassium cyanide 350-30-1, 3-Chloro-4-fluoronitrobenzene 350-46-9, 4-Fluoronitrobenzene 358-23-6, Trifluoromethanesulfonic anhydride 407-25-0, Trifluoroacetic anhydride 446-33-3, 5-Fluoro-2-nitrotoluene 506-59-2, Dimethylamine hydrochloride 515-74-2, Sodium sulfanilate 540-51-2, 2-Bromoethanol 556-48-9, 1,4-Cyclohexanediol 577-19-5, 2-Bromonitrobenzene 589-10-6, 2-Phenoxyethyl bromide 591-97-9, 1-Chloro-2-butene 615-53-2, N-Methyl-N-nitrosourethane 619-24-9, 3-Nitrobenzonitrile 624-76-0, 2-Iodoethanol 625-36-5, 3-Chloropropionyl chloride 626-88-0, 1-Bromo-4-methylpentane 646-07-1, 4-Methylvaleric acid 654-76-2, 2-Methoxy-5-nitrobenzotrifluoride 697-82-5, 2,3,5-Trimethylphenol 872-85-5, Isonicotinaldehyde 930-68-7, 2-Cyclohexen-1-one 934-22-5, 1H-Benzimidazol-5-amine 1072-72-6, Tetrahydrothiopyran-4-one 1073-13-8, 4,4-Dimethyl-2-cyclohexen-1-one 1194-02-1, 4-Fluorobenzonitrile 1759-53-1, Cyclopropanecarboxylic acid 2081-44-9, 4-Hydroxytetrahydropyran 2201-24-3, 1-Phenylcyclohexylamine 2615-25-0, trans-1,4-Diaminocyclohexane 2759-28-6, 1-Benzylpiperazine 3096-69-3, 2,3-Dimethyl-4-aminophenol 3251-56-7, 2-Methoxy-4-nitrophenol 3282-30-2, Pivaloyl chloride 3385-21-5, 1,3-Diaminocyclohexane 3612-20-2, 1-Benzyl-4-piperidone 4376-18-5, Phthalic acid monomethyl ester 4635-59-0, 4-Chlorobutyryl chloride 4908-50-3 5006-62-2, Ethyl 3-piperidinecarboxylate 5401-94-5, 5-Nitroindazole 5414-19-7, Bis(2-bromoethyl) ether 5460-31-1, 3-Nitro-o-cresol 6051-66-7, 2,5-Dimethylterephthalic acid 6436-90-4, N-Benzylglycine ethyl ester 6482-24-2, 2-Bromoethyl methyl ether 6859-99-0, 3-Hydroxypiperidine 6936-47-6, cis-2-Aminocyclohexanol hydrochloride 6967-12-0, 1H-Indazol-6-amine 7486-35-3, Tributylvinyltin 7664-41-7, Ammonia, reactions 7803-49-8, Hydroxylamine, reactions 10315-07-8, 1-Benzyl-4-piperidinecarboxylic acid 13139-17-8, 1-[[(Benzyloxy)carbonyl]oxy]-2,5-pyrrolidinedione 14660-52-7, Ethyl 5-bromovalerate 17159-80-7, Ethyl 4-hydroxycyclohexanecarboxylate 17449-76-2, Methyl 4-hydroxycyclohexanecarboxylate 18162-48-6, tert-Butyldimethylsilyl chloride 18595-14-7, Methyl 4-amino-3-methylbenzoate 19335-11-6, 5-Aminoindazole 19438-10-9, 3-Hydroxybenzoic acid methyl ester 19499-93-5, 2,3-Dimethyl-4-nitrophenol 22509-74-6, N-Carboethoxyphthalimide 24424-99-5, Di-tert-butyl dicarbonate 25912-50-9, 3-Aminocyclohexanecarboxylic acid 26386-88-9, Diphenylphosphoryl azide 27489-62-9, trans-4-Aminocyclohexanol 30525-89-4, Paraformaldehyde 33024-60-1, Tetrahydro-2H-pyran-4-ylamine monohydrochloride 50593-24-3, 1-Methyl-1H-indazol-5-amine 51535-00-3, Methyl 1-benzyl-5-oxo-3-pyrrolidinecarboxylate 53857-57-1, 5-Bromo-1H-indazole 54288-70-9, 4-Bromopiperidine hydrobromide 59247-47-1, tert-Butyl-4-bromobenzoate 59719-74-3, 1,3-Cyclopentanediol 60206-30-6, 8-Propyl-8-azabicyclo[3.2.1]octan-3-one 60518-59-4, 2-Methyl-2H-indazol-5-amine 63301-31-5 74626-47-4, 1H-Indazole-5-carbonitrile 76445-65-3, 4-Aminocyclohexanol hydrochloride 81029-03-0, 2,3-Dimethyl-4-nitroanisole 84358-13-4, 1-(tert-Butoxycarbonyl)-4-piperidinecarboxylic acid 97181-50-5 99799-10-7 103057-44-9, tert-Butyl 3-hydroxypyrrolidine-1-carboxylate 109384-19-2, tert-Butyl 4-hydroxypiperidine-1-carboxylate 132302-53-5, 2-(1H-Indazol-5-ylamino)benzoic acid 215120-68-6, 4-([[(Benzyloxy)carbonyl]amino]methyl)cyclohexanecarboxylic acid 239097-74-6, 1,2-Benzisoxazol-5-amine 248924-30-3 261762-91-8

280772-00-1, 1-(Methylsulfonyl)-4-piperidinecarboxylic acid 478841-81-5
478920-45-5
(preparation of heterocyclic compds. as Rho-kinase inhibitors)
IT 3385-21-5, 1,3-Diaminocyclohexane
(preparation of heterocyclic compds. as Rho-kinase inhibitors)
RN 3385-21-5 USPATFULL
CN 1,3-Cyclohexanediamine (CA INDEX NAME)



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NUMBER OF CLAIMS: 58
EXEMPLARY CLAIM: 1
LINE COUNT: 6512
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides compounds comprising a bicyclic aryl moiety, such as 2H-phthalazin-1-one or derivatives thereof, compositions comprising

the same, and methods for producing and using the same. In particular, the present invention provides compounds of the formula: ##STR1##

or a pharmaceutically acceptable salt, a hydrate, a solvate, or a prodrug thereof; where Q.sup.1, Q.sup.2 and Y are those defined herein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . prepared according to the modified procedures of Swain, C. J. et al., J. Med. Chem. 1991, 34, 140-151. Briefly, hydroxylamine hydrochloride (0.15 g, 2.1 mmol) and Na.sub.2CO.sub.3 (0.11 g, 1.05 mmol) were dissolved in 20% H.sub.2O in EtOH, followed by addition. . .

DETD [0410] Hydroxylamine hydrochloride (0.50 g, 7.22 mmol) and Na.sub.2CO.sub.3 (0.38 g, 3.61 mmol) were dissolved in 2.5 mL water. A solution of 6-chloronicotinonitrile. . .

DETD [0422] Hydroxylamine hydrochloride (179 mg, 2.60 mmol) and Na.sub.2CO.sub.3 (138 mg, 1.30 mmol) was dissolved in 1 mL water. A solution of (3-cyano-phenyl)-carbamic. . .

DETD [0428] Hydroxylamine hydrochloride (104 mg, 1.5 mmol) and Na.sub.2CO.sub.3 (80 mg, 0.75 mmol) were dissolved in 0.5 mL of water. A solution of. . .

DETD [0434] Hydroxylamine hydrochloride (100 mg, 1.44 mmol) and Na.sub.2CO.sub.3 (76 mg, 0.72 mmol) were dissolved in 0.5 mL of water. A solution of. . .

DETD . . . (124 mg, 0.50 mmol) and 4-(3-amino-propylamino)-2H-phthalazin-1-one (100 mg, 0.46 mmol) were dissolved in DMF (2 mL) and treated with 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (95 mg, 0.50 mmol) and triethylamine (76 mg, 0.75 mmol). 3-[5-(4-Methoxy-phenyl)-isoxazol-3-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide was isolated by preparative RPLC.

DETD . . . was then cooled to ambient temperature. In a second 1-L, one-neck, round bottomed flask equipped with a magnetic stirrer, 2-dimethylaminoethylchloride hydrochloride (13.2 g, 0.300 mol) was slurried in toluene (200 mL), and saturated aqueous potassium carbonate (400 mL) added. The mixture. . .

DETD [0566] In a second 100-mL, one-neck, round bottomed flask equipped with a magnetic stirrer, 2-dimethylaminoethylchloride hydrochloride (4.32 g, 30.0 mmol) was slurried in toluene (20 mL), and saturated aqueous potassium carbonate (35 mL) added. The mixture. . .

DETD . . . with a magnetic stirrer and a reflux condenser was charged with 4-(2-dimethylaminoethoxy)benzonitrile (31.5 g, 0.17 mol), ethanol (200 mL), hydroxylamine hydrochloride (17.2 g, 0.25 mol) and potassium carbonate (34.8 g, 0.25 mol). The resulting mixture was refluxed for 18 h. After. . .

DETD . . . bottom flask equipped with a magnetic stirrer and reflux condenser was charged with methyl 3-[3-(1-methyl-1H-pyrrol-2-yl)-1,2,4-oxadiazol-5-yl]propionate (2.14 g, 9.10 mmol), dimethylamine hydrochloride (2.20 g, 27.0 mmol), paraformaldehyde (0.82 g, 27.0 mmol) and n-butanol (80 mL). The mixture was heated to 100° C. for 16 h. After this time, additional dimethylamine hydrochloride (1.10 g, 13.5 mmol) and paraformaldehyde (0.41 g, 13.5 mmol) were added and heating continued for 8 h. The reaction. . .

DETD [0641] This example illustrates a method for producing hydrochloride salt of N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-3-(3-p-tolyl-[1,2,4]oxadiazol-5-yl)-propionamide. ##STR1299##

DETD . . . nitrogen and charged with 4-(3-aminopropylarnino)-2H-phthalazin-1-one (152 mg, 0.65 mmol), 3-{3-[4-methylphenyl]-1,2,4-oxadiazol-5-yl}propionic acid (163 mg, 0.65 mmol), anhydrous DMF (4 mL),

1-(3-dimethylamino-propyl)-3-ethylcarbodiimide hydrochloride (150 mg, 0.78 mmol), 1-hydroxybenzotriazole (84 mg, 0.78 mmol) and diisopropylethylamine (85 mg, 0.78 mmol). After stirring for 22 h. . . filtrate was concentrated to dryness under reduced pressure. The residue was purified by column chromatography and converted to the corresponding hydrochloride salt by treatment of a methanol (2 mL) suspension of the free base with one equivalent of a 1 M. . .

DETD [0644] Hydrochloride salt of 3-[3-(4-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 84%, white solid; m.p. 198-200° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.55 (s, 1H), 8.20 (d, 1H,. . .

DETD [0645] Hydrochloride salt of N-[3-(4-Oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-3-(3-phenyl-[1,2,4]oxadiazol-5-yl)-propionamide, 62%, white solid; m.p. 179-181 ° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.55 (s, 1H), 8.20 (d,. . .

DETD [0646] Hydrochloride salt of N-[3-(4-Oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-3-(3-p-tolyl-[1,2,4]oxadiazol-5-yl)-propionamide, 53%, white solid; m.p. 194-196° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.54 (s, 1H), 8.21 (d, 1H,. . .

DETD [0647] Hydrochloride salt of 3-[3-(4-Methoxy-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-cyclohexyl]-propionamide, 79%, off-white solid; m.p. 155° C. (dec.); .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.52 (s, 1H), 8.18 (m,. . .

DETD [0648] Hydrochloride salt of N-[3-(4-Oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-3-[3-(4-trifluoromethoxy-phenyl)-[1,2,4]oxadiazol-5-yl]-propionamide, 25%, white solid; m.p. 176-179° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.55 (s, 1H), 8.22 (d, 1H,. . .

DETD [0649] Hydrochloride salt of 3-[3-(4-Fluoro-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 30%, white solid; m.p. 284-287° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 8.24 (d, 11H, J=7.1 Hz), 7.82-8.05. . .

DETD [0650] Hydrochloride salt of 3-[3-(2,3-Dihydro-benzofuran-5-yl)-[1,2,4]oxadiazol-5-yl]-N-[2,2-dimethyl-3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 82%, white solid; m.p. 115-118° C.; .sup.1H NMR (CDCl.sub.3) δ (ppm) 9.28 (bs, 1H), 8.42 (m, 2H),. . .

DETD [0651] Hydrochloride salt of 2-Hydroxy-N-[2-hydroxy-3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-4-methylsulfanyl-butyramide, 66%, white solid; m.p. 165-170° C.; 1H NMR (DMSO-d.sub.6) δ (ppm) 11.56 (s, 1H), 8.22 (dd, 1H,. . .

DETD [0652] Hydrochloride salt of 3-(3-Benzo[1,3]dioxol-5-yl-[1,2,4joxadiazol-5-yl)-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 69%, white solid; m.p. 236-242° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.53 (s, 1H), 8.21 (d, 1H,. . .

DETD [0653] Hydrochloride salt of N-[3-(4-Oxo-3,4-dihydro-phthalazin-1-ylamino)-porpyl]-3-(3-thiophen-2-yl-[1,2,4]oxadiazol-5-yl)-propionamide, 83%, tan solid; m.p. 193-196° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.57 (s, 1H), 8.20 (d, 1H,. . .

DETD [0654] Hydrochloride salt of 3-[3-(2,3-Dichloro-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 79%, off-white solid; m.p. 178-184° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.55 (s, 11H), 8.21 (d, 1. . .

DETD [0655] Hydrochloride salt of 3-[3-(4-Methylsulfanyl-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 77%, white solid; m.p. 190-191° C.; .sup.1H NMR (CD.sub.3OD) δ (ppm) 8.28 (m, 2H), 8.02 (m, 2H),. . .

DETD [0656] Hydrochloride salt of 3-[3-(2,3-Dihydro-benzofuran-5-yl)-[1,2,4]oxadiazol-5-yl]-N-[2-hydroxy-3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 33%, white solid; m.p. 174-177° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.55 (s, 1H), 8.21 (dd, 1H,. . .

DETD [0657] Hydrochloride salt of 3-[3-(6-Methoxy-pyridin-3-yl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 49%, pink solid; m.p. 150° C. (dec.); .sup.1H NMR (CD.sub.3OD) δ (ppm) 8.68 (d, 1H, J=2.2 Hz),. . .

DETD [0658] Hydrochloride salt of N-[3-(4-Oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-3-(3-thiophen-3-yl-[1,2,4]oxadiazol-5-yl)-propionamide, 64%, white solid; m.p. 195-198° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.57 (s, 1H), 8.23 (m, 2H),. . .

DETD [0659] Hydrochloride salt of 3-[3-[4-(2-Dimethylamino-ethoxy)-phenyl]-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 17%, white solid; m.p. 65-67° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.54 (s, 1H), 10.10 (s, 1H),. . .

DETD [0660] Hydrochloride salt of 3-[3-(4-Hydroxy-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(5-oxo-5,6-dihydro-pyrido[2,3-d]pyridazin-8-ylamino)-cyclohexyl]-propionamide, 14%, yellow solid; m.p. 74° C. (dec.); .sup.1H NMR (CD.sub.3OD) δ (ppm) 9.02 (dd, 1H, J=1.6, 4.6. . .

DETD [0661] Hydrochloride salt of 3-[3-(4-Difluoromethoxy-phenyl)-[1,2,4joxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 49%, off-white solid; m.p. 189-196° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.55 (s, 1H), 8.30-7.70 (m, 7H),. . .

DETD [0662] Hydrochloride salt of 3-[3-(4-Bromo-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 24%, white solid; m.p. 188-195° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.57 (bs, 1H), 8.08-8.34 (m, 3H),. . .

DETD [0663] Hydrochloride salt of N-[3-(5, 8-Difluoro-4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-3-[3-(4-methoxy-phenyl)-[1,2,4]oxadiazol-5-yl]-propionamide, 14%, pale yellow solid; m.p. 174-176° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.66 (s, 1H), 8.10. . .

DETD [0664] Hydrochloride salt of 3-{3-[3-(2-Dimethylamino-ethoxy)-phenyl]-[1,2,4]oxadiazol-5-yl}-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 32%, white solid; m.p. 68-70° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.57 (s, 1H), 10.32 (s, 1H),. . .

DETD [0665] Hydrochloride salt of 3-[3-(4-Dimethylaminomethyl-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 55%, white solid; m.p. 98° C. (dec.); .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.56 (s, 1H), 11.26 (s,. . .

DETD [0666] Hydrochloride salt of 3-[3-(3-Dimethylaminomethyl-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 24%, white solid; m.p. 90° C. (dec.); .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.54 (s, 1H), 10.74 (s,. . .

DETD [0667] Hydrochloride salt of 3-[3-(3-Hydroxy-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 31%, white solid; m.p. 250-251° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.54 (s, 1H), 8.21 (d, 1H,. . .

DETD [0668] Hydrochloride salt of 3-[3-(3,4-Difluoro-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 55%, off-white solid; m.p. 195-200° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.53 (s, 1H), 8.20 (d, 1H,. . .

DETD [0669] Hydrochloride salt of 3-[3-(3,4-Dihydroxy-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-

propyl]-propionamide, 45%, light brown solid; m.p. 178-185° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.54 (s, 1 H), 8.20. . .

DETD [0670] Hydrochloride salt of 3-[3-(3,5-Dihydroxy-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 39%, off-white solid; m.p. 189-195° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.52 (s, 1H), 8.22 (d, 1H,. . .

DETD [0671] Hydrochloride salt of 3-[3-(2, 3-Dihydroxy-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 41%, off-white solid; m.p. 178-182° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.55 (s, 1H), 8.20 (d,. . .

DETD [0672] Hydrochloride salt of 3-[3-(2,5-Dihydroxy-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 60%, white solid; m.p. 200-206° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.55 (s, 1H), 8.21 (d,. . .

DETD [0673] Hydrochloride salt of 3-[3-(2,4-Dihydroxy-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 28%, white solid; m.p. 202° C. (dec.); .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.57 (s, 1H), 8.10-8.20 (m,. . .

DETD [0674] Hydrochloride salt of 3-[3-(2,6-Dihydroxy-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 57%, white solid; m.p. 170-172° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.56 (s, 1H), 10.82 (s, 1H),. . .

DETD [0675] Hydrochloride salt of 3-[3-(1-Methyl-1H-pyrrol-2-yl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 74%, yellow solid; m.p. 173-177° C. (dec.); .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.56 (bs, 1H), 8.10-8.20 (m,. . .

DETD [0676] Hydrochloride salt of 3-{3-[4-(2-Morpholin-4-yl-ethoxy)-phenyl]-[1,2,4]oxadiazol-5-yl}-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 63%, tan solid; m.p. 114-116° C.; .sup.1H NMR (CD.sub.3OD) δ (ppm) 7.84-8.29 (m, 6H), 6.94 (d, 2H,. . .

DETD [0677] Hydrochloride salt of 3-[3-(6-Hydroxy-pyridin-3-yl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 41%, tan solid; m.p. 153° C. (dec.); .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 8.15-8.23(m, 3H), 7.97 (d, 1H,. . .

DETD [0678] Hydrochloride salt of 3-[3-(2,3-Dimethoxy-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 45%, white solid; m.p. 137-144° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.54 (s, 1H), 8.08 (t, 2H,. . .

DETD [0679] Hydrochloride salt of 3-[3-(2,4-Dimethoxy-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 58%, white solid; m.p. 120° C. (dec.); .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.55 (s, 1H), 8.21 (d,. . .

DETD [0680] Hydrochloride salt of 3-[3-(2,5-Dimethoxy-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 66%, off-white solid; m.p. 198-201° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.61 (s, 1H), 8.20 (d, 1H. . .

DETD [0681] Hydrochloride salt of 3-[3-(2, 6-Dimethoxy-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 39%, off-white solid; m.p. 171-176° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.71 (s, 1H), 8.20. . .

DETD [0682] Hydrochloride salt of 3-[3-(2,6-Dimethoxy-4-methyl-pyridin-3-yl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-

propyl]-propionamide, 49%, white solid; m.p. 105° C. (dec.); .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.55 (s, 1H), 8.21 (d,. . .

DETD [0683] Hydrochloride salt of 3-{3-[1-(2-Dimethylamino-ethyl)-1H-pyrrol-2-yl]-[1,2,4]oxadiazol-5-yl}-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide 77%, white solid; m.p. 110-111° C.; .sup.1H NMR (CD.sub.3OD) δ (ppm) 8.31 (d, 1H, J=7.6 Hz), 8.00. . .

DETD [0686] Hydrochloride salt of N-[3-(4-Oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-3-(3-piperidin-4-yl-[1,2,4]oxadiazol-5-yl)-propionamide, 80%, white solid; m.p. 107-109° C.; .sup.1H NMR (CD.sub.3OD) δ (ppm) 8.32 (dd, 1H, J=1.4, 8.0 Hz),. . .

DETD [0687] Hydrochloride salt of 3-[3-(5-Dimethylaminomethyl-1-methyl-1H-pyrrol-2-yl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 33%, Orange solid; m.p. 87-91 (dec.); .sup.1H-NMR (DMSO-d.sub.6) δ (ppm) 11.54 (s, 1H), 8.21 (d, 1H, J=7.7. . .

DETD [0688] Hydrochloride salt of 3-[3-[2-(4-Methyl-piperazin-]-yl)-pyridin-3-yl]-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 65%, yellow solid; m.p. 75° C. (dec.); .sup.1H NMR (CD.sub.3OD) δ (ppm) 8.26-8.33 (m, 3H), 7.81-7.97 (m,. . .

DETD [0689] Hydrochloride salt of 3-[3-(1-Methyl-piperidin-2-yl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 59%, yellow solid; m.p. 125° C. (dec.); .sup.1H NMR (CD.sub.3OD) δ (ppm) 8.33 (d, 1H, J=7.5 Hz),. . .

DETD [0690] Hydrochloride salt of 3-[3-(1-Methyl-pyrrolidin-2-yl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 10%, white solid; m.p. 65-67° C.; .sup.1H NMR (CD.sub.3OD) δ (ppm) 8.30 (m, 2H), 7.97 (m, 2H),. . .

DETD [0691] Hydrochloride salt of 3-[3-(1-Methyl-piperidin-3-yl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 20%, yellow solid; m.p. 135° C. (dec.); .sup.1H NMR (CD.sub.3OD) δ (ppm) 8.33 (d, 1H, J=7.7Hz), 8.03. . .

DETD [0692] Hydrochloride salt of N-[3-(4-Oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-3-{3-[3-(2,2,2-trifluoro-ethoxy)-phenyl]-[1,2,4]oxadiazol-5-yl}-propionamide, 84%, off-white solid; m.p. 152-158° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.55 (s, 1H), 8.22 (d, 1H,. . .

DETD [0693] Hydrochloride salt of N-[3-(4-Oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-3-{3-[4-(2,2,2-trifluoro-ethoxy)-phenyl]-[1,2,4]oxadiazol-5-yl}-propionamide, 67%, Off-white solid; m.p. 192-196° C. (dec.); .sup.1H-NMR (DMSO-d.sub.6) δ (ppm) 11.56 (s, 1H), 8.20 (d, 1H,. . .

DETD [0694] Hydrochloride salt of 3-[3-(3-Fluoro-4-methyl-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 46%, off-white solid; m.p. 185-190° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.54 (bs, 1H), 8.22-8.17 (m, 3H),. . .

DETD [0695] Hydrochloride salt of 3-[3-(4-Isopropoxy-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 87%, off-white solid; m.p. 183-186° C. (dec.); .sup.1H-NMR (DMSO-d.sub.6) δ (ppm) 11.56 (bs, 1H), 8.21 (d, 1H,. . .

DETD [0696] Hydrochloride salt of 3-[3-(4-Cyclopropylmethoxy-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 97%, off-white solid; m.p. 178-180° C.

(dec.); .sup.1H-NMR (DMSO-d.sub.6) δ (ppm) 11.56 (bs, 1H), 8.14-8.22 (m, 3H),. . .

DETD [0697] Hydrochloride salt of 3-[3-(3-Isopropoxy-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 86%, off-white solid; m.p. 135-141° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 8.30-8.19 (m, 3H), 7.86 (m, 2H),. . .

DETD [0698] Hydrochloride salt of N-[3-(4-Oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-3-[3-(5-propionylamino-thiophen-3-yl)-[1,2,4]oxadiazol-5-yl]-propionamide, 71%, off-white solid; m.p. 112-114° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.56 (s, 1H), 11.33 (s, 1H),. . .

DETD [0699] Hydrochloride salt of 3-Methyl-N-[4-(5-[{2-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propylcarbamoyl]-ethyl}-[1,2,4]oxadiazol-3-yl)-thiophen-2-yl]-butyramide, 66%, white solid; m.p. 137-139° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.56 (s, 1H), 11.34 (s, 1H),. . .

DETD [0700] Hydrochloride salt of 3-[3-(4-Methoxymethyl-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 73%, white solid; m.p. 183° C. (dec.); .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.55 (s, 1H) 8.21 (d,. . .

DETD [0701] Hydrochloride salt of 3-[3-(3-Methoxy-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 62%, off-white solid; m.p. 166-172° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.56 (s, 1H), 8.21 (d, 1H,. . .

DETD [0702] Hydrochloride salt of 3-[3-(3-Ethoxy-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 54%, off-white solid; m.p. 166-171° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.55 (bs, 1H), 8.21 (d, 1H,. . .

DETD [0703] Hydrochloride salt of 3-[3-(3-Chloro-4-methyl-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 49%, yellow solid; m.p. 185-187° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.53 (s, 1H), 8.20 (d, 1H,. . .

DETD [0704] Hydrochloride salt of 3-[3-(1-Ethyl-1H-pyrrol-2-yl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 57%, off-white solid; m.p. 148-150 (dec.); .sup.1H-NMR (DMSO-d.sub.6) 6 (ppm) 11.55 (bs, 1H), 8.21 (d, 1H, J=7.8. . .

DETD [0705] Hydrochloride salt of N-[3-(4-Oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-3-[3-(3-propoxy-phenyl)-[1,2,4]oxadiazol-5-yl]-propionamide, 64%, off-white solid; m.p. 141-149 (dec.); .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.55 (s, 1H), 8.22 (d, 1H,. . .

DETD [0706] Hydrochloride salt of N-[3-(4-Oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-3-[3-(4-propoxy-phenyl)-[1,2,4]oxadiazol-5-yl]-propionamide, 87%, off-white solid; m.p. 193-196° C. (dec.), .sup.1H-NMR (DMSO-d.sub.6) δ (ppm) 11.56 (bs, 1H), 8.21 (d, 1H,. . .

DETD [0707] Hydrochloride salt of 3-[3-(4-Ethoxy-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 45%, off-white solid; m.p. 196-199° C. (dec.); .sup.1H-NMR (DMSO-d.sub.6) δ (ppm) 11.55 (bs, 1H), 8.20 (d, 1H,. . .

DETD [0708] Hydrochloride salt of 3-[3-(3-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 60%, off-white solid; m.p. 195-198° C. (dec.); .sup.1H-NMR (DMSO-d.sub.6) δ (ppm) 11.55 (bs, 1H), 8.20 (d, 1H,. . .

DETD [0709] Hydrochloride salt of 3-[3-(2-Ethyl-thiophen-3-yl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 69%, off-white solid; m.p. 156-160° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.57 (bs, 1H), 8.21 (d, 1H,. . .

DETD [0710] Hydrochloride salt of 3-[3-(3-Ethoxymethyl-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 61%, white solid; m.p. 155-157° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.55 (s, 1H), 8.21 (d, 1H,. . . .

DETD [0711] Hydrochloride salt of 3-{3-[1-(2-Ethoxy-ethyl)-1H-pyrrol-2-yl]-[1,2,4]oxadiazol-5-yl}-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 54%, off-white solid; m.p. 139-143° C. (dec.); .sup.1H-NMR (DMSO-d.sub.6) δ (ppm) 8.18-8.23 (m, 3H), 7.92 (m, 2H),. . . .

DETD [0712] Hydrochloride salt of 3-[3-(3-Ethyl-phenyl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 23%, off-white solid; m.p. 168-170° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.55 (s, 1H), 8.21 (dd, 1H,. . . .

DETD [0713] Hydrochloride salt of 3-[3-(5-Ethanesulfonylamino-thiophen-3-yl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 64%, white solid; m.p. 161° C. (dec.); .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.56 (s, 1H), 10.57 (s,. . . .

DETD [0714] Hydrochloride salt of 3-{3-[5-(3-Isobutyl-ureido)-thiophen-3-yl]-[1,2,4]oxadiazol-5-yl}-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 60%, off-white solid; m.p. 143-145° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.57 (bs, 1H), 9.89 (s, 1H),. . . .

DETD [0715] This example illustrates a method for producing hydrochloride salt of 3-{3-[1-(2-Hydroxy-ethyl)-1H-pyrrol-2-yl]-[1,2,4]oxadiazol-5-yl}-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide. ##STR1300##

DETD . . . resulting solid purified by column chromatography. The resulting material was suspended in methanol (5 mL) and converted to the corresponding hydrochloride salt by treatment with one equivalent of a 1 M solution of hydrogen chloride in diethyl ether. Concentration of the. . .

DETD . . . nitrogen and charged with 4-(3-aminopropylamino)-2H-phthalazin-1-one (451 mg, 2.07 mmol), 3-[3-(5-tert-butyloxycarbonylamino-3-methylisoxazol-4-yl)-1,2,4-oxadiazol-5-yl]propionic acid (699 mg, 2.07 mmol), anhydrous DMF (7 mL), 1-(3-dimethylamino-propyl)-3-ethylcarbodiimide hydrochloride (595 mg, 3.10 mmol), 1-hydroxybenzotriazole (221 mg, 2.07 mmol) and diisopropylethylamine (320 mg, 2.48 mmol). After stirring for 17 h. . .

DETD . . . the free base as an off-white solid. This solid was dissolved in methanol (3 mL) and converted to the corresponding hydrochloride salt by treatment with one equivalent of a 1 M hydrogen chloride solution in ether and concentration of the resulting. . .

DETD [0748] This example illustrates a method for producing hydrochloride salt of N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-3-(3-piperidin-4-yl-[1,2,4]oxadiazol-5-yl)-propionamide. ##STR1303##

DETD . . . carbonate solution and the mixture re-evaporated to dryness. The residue was purified by column chromatography and converted to the corresponding hydrochloride salt by treatment of a methanol (5 rnL) solution of the free base with one equivalent of a 1 M. . .

DETD [0751] 3-[3-(4-Amino-2-methylsulfanyl-thiazol-5-yl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide Hydrochloride, 99%, light yellow solid; m.p. 141° C. (dec.); .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.61 (bs, 1H), 8.18-8.23 (m,

3H), 7.87. . .

DETD [0752] Hydrochloride salt of N-[3-(4-Oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-3-(3-piperidin-2-yl-[1,2,4]oxadiazol-5-yl)-propionamide, 71%, yellow solid; m.p. 130° C. (dec.), .sup.1H NMR (CD.sub.3OD) (ppm) 8.33 (d, 1H, J=7.4 Hz), 7.80-8.10. . .

DETD [0753] Hydrochloride salt of N-[3-(4-Oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-3-(3-pyrrolidin-2-yl-[1,2,4]oxadiazol-5-yl)-propionamide, 99%, white solid; m.p. 73-75° C.; .sup.1H NMR (CD.sub.3OD) δ (ppm) 8.33 (dd, 1H, J=1.1, 7.9 Hz),. . .

DETD [0754] Hydrochloride salt of N-[3-(4-Oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-3-(3-piperidin-3-yl-[1,2,4]oxadiazol-5-yl)-propionamide, 89%, yellow solid; m.p. 157° C. (dec.), .sup.1H NMR (CD.sub.3OD) δ (ppm) 7.92-8.40 (m, 4H), 3.25-3.65 (m,. . .

DETD [0755] Hydrochloride salt of 3-[3-(5-Amino-1-methyl-1H-pyrazol-4-yl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide, 88%, white solid; m.p. 173° C. (dec.); .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 11.53 (bs, 1H), 8.16-8.23 (m,. . .

DETD [0756] Hydrochloride salt of 3-[3-(5-Amino-3H-imidazol-4-yl)-[1,2,4]oxadiazol-5-yl]-N-[3-(4-oxo-3,4-dihydro-phthalazin-1-ylamino)-propyl]-propionamide was synthesized in a similar fashion, but an equal volume of 4 N hydrochloric acid and methanol. . .

DETD . . . acid anhydrides or chlorides, including the observed yield and analytical data, are listed below. Compounds that were isolated as the hydrochloride salt, were obtained from the corresponding free base as described above.

DETD [0761] Hydrochloride salt of N-[3-(4-Oxo-3,4-dihydro-phthalazin-1-ylamino)-cyclohexyl]-oxalamic acid ethyl ester, 62%, white solid; m.p. 178-182° C.; .sup.1H NMR (CD.sub.3OD) δ (ppm) 8.65 (d, 1H,. . .

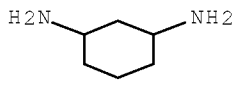
DETD [0765] Hydrochloride salt of N-[3-(4-Oxo-3,4-dihydro-phthalazin-1-ylamino)-cyclohexyl]-propionamide, 48%, off-white solid; m.p. 197-201° C.; .sup.1H NMR (DMSO-d.sub.6) δ (ppm) 8.25-7.70 (m, 4H) 3.60 (m, 2H),. . .

IT 75-26-3, 2-Bromopropane 85-44-9, Phthalic anhydride 100-52-7, Benzaldehyde, reactions 108-30-5, Succinic anhydride, reactions 109-01-3, 1-Methylpiperazine 109-76-2, 1,3-Propanediamine 110-60-1, Butane-1,4-diamine 110-91-8, Morpholine, reactions 123-75-1, Pyrrolidine, reactions 501-53-1, Benzyl chloroformate 536-40-3, 4-Chlorobenzoyl hydrazide 592-55-2, 1-Bromo-2-ethoxyethane 699-98-9, 2,3-Pyridinedicarboxylic anhydride 767-00-0, 4-Cyanophenol 768-60-5, 1-Ethynyl-4-methoxybenzene 874-89-5, 4-Hydroxymethylbenzonitrile 950-81-2, 4-Antipyrinecarboxaldehyde 1490-25-1, 3-Carbomethoxypropionyl chloride 1641-09-4, Thiophene-3-carbonitrile 2237-30-1, 3-Aminobenzonitrile 2623-87-2, 4-Bromobutyric acid 3385-21-5, 1,3-Cyclohexanediamine 3878-55-5, Monomethyl succinate 4513-94-4, Pyrrole-2-carbonitrile 4584-46-7, 2-Dimethylaminoethyl chloride hydrochloride 4733-65-7, 3-Carbamoylpicolinic acid 4744-50-7, 2,3-Pyrazinedicarboxylic anhydride 5334-41-8, 5-Amino-1-methyl-1H-pyrazole-4-carbonitrile 5444-02-0, 2,6-Dihydroxy-4-methylnicotinonitrile 5860-70-8, 2-Carbamylnicotinic acid 6587-24-2, 2-Cyanobenzoic acid methyl ester 7328-91-8, 2,2-Dimethylpropane-1,3-diamine 13013-02-0, Methyl 4-nitrobutyrate 13154-24-0, Triisopropylchlorosilane 17201-43-3, 4-Bromomethylbenzonitrile 20215-79-6 21382-98-9, 4-Methylsulfanylbenzonitrile 24424-99-5, Di-tert-butyl dicarbonate 31469-15-5, [(1-Methoxy-2-methylpropenyl)oxy]trimethylsilane 33252-28-7, 6-Chloronicotinonitrile 36239-09-5, Ethyl malonyl chloride 57260-73-8, (2-Aminoethyl)carbamic acid tert-butyl ester 76513-69-4, 2-Chloromethoxyethyltrimethylsilane

87517-47-3, Methyl 4-azidobutanoate 108078-14-4, 2-Iodo-3-methylbenzoic acid 159824-95-0, 5-Aminothiophene-3-carbonitrile 162167-97-7, 3-(Aminomethyl)-1-(tert-butoxycarbonyl)piperidine 500024-16-8, 2,2-Dimethyl-2,3-dihydro-1H-4,9a-diazafluoren-9-one 500024-31-7 500024-36-2, 3-[5-(4-Methoxyphenyl)isoxazol-3-yl]propionic acid methyl ester 500024-67-9
(preparation of phthalazinone PARP inhibitors for treatment of cancer)

IT 3385-21-5, 1,3-Cyclohexanediamine
(preparation of phthalazinone PARP inhibitors for treatment of cancer)

RN 3385-21-5 USPATFULL
CN 1,3-Cyclohexanediamine (CA INDEX NAME)



L79 ANSWER 25 OF 38 USPATFULL on STN

ACCESSION NUMBER:	2004:101796 USPATFULL Full-text		
TITLE:	Nitrogen substituted biaryl purine derivatives as potent antiproliferative agents		
INVENTOR(S):	Trova, Michael Peter, Schenectady, NY, UNITED STATES		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004077666	A1	20040422
	US 6949559	B2	20050927
APPLICATION INFO.:	US 2003-680832	A1	20031007 (10) <--
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2001-950543, filed on 11 Sep 2001, GRANTED, Pat. No. US 6667311		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	Nixon Peabody LLP, Clinton Square, P.O. Box 31051, Rochester, NY, 14603-1051		
NUMBER OF CLAIMS:	13		
EXEMPLARY CLAIM:	1		
LINE COUNT:	6457		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The compounds of the present invention are 2,6,9-trisubstituted purine derivatives which are inhibitors of cyclin/cdk complexes. The compounds of the current invention also are potent inhibitors of human cellular proliferation. As such, the compounds of the present invention constitute pharmaceutical compositions with a pharmaceutically acceptable carrier. Such compounds are useful in treating a disorder mediated by elevated levels of cell proliferation in a mammal compared to a healthy mammal by administering to such mammal an effective amount of the compound. Examples of the compounds of the present invention are represented by the following chemical structures: ##STR1##

with X, Y, D, Q, V, A, R.sub.1, R.sub.2, R.sub.3, R.sub.4, and n.sub.1 defined herein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD [1404] To compound 4 (0.12 g, 0.27 mmol) was added 3-aminophenylboronic

acid hydrochloride (0.12 g, 0.69 mmol), and Pd(PPh.sub.3).sub.4 (0.09 g, 0.75 mmol) in a sealed tube filled with argon. To this mixture. . .

DETD [1414] To compound 3 (0.26 g, 0.67 mmol) was added trans-4-aminocyclohexanol hydrochloride (0.62 g, 4.11 mmol), Et.sub.3N (0.58 mL, 4.16 mmol), and ethanol (5 mL). The mixture was heated for 5 h. . .

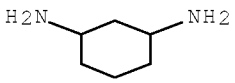
DETD [1435] Compound 72 (0.15 g, 0.40 mmol), trans-4-aminocyclohexanol hydrochloride (0.31 g, 1.99 mmol), Et.sub.3N (0.11 mL, 0.8 mmol), and EtOH (5 mL) were combined and heated in a sealed tube at 155° C. for 4 d. Additional trans-4-aminocyclohexanol hydrochloride (0.34 g, 2.2 mmol) and triethylamine (0.60 mL, 4.3 mmol) were added and the heat was resumed at 155° C.. . .

IT 75-30-9 92-69-3, [1,1'-Biphenyl]-4-ol 92-92-2, [1,1'-Biphenyl]-4-carboxylic acid 98-80-6 103-71-9, reactions 107-08-4, 1-Iodopropane 107-15-3, 1,2-Ethanediamine, reactions 108-30-5, Succinic anhydride, reactions 109-04-6 109-76-2, 1,3-Propanediamine 110-60-1, 1,4-Butanediamine 123-38-6, Propionaldehyde, reactions 123-72-8, Butyraldehyde 513-48-4, 2-Iodobutane 605-65-2 619-58-9 623-00-7 624-28-2, 2,5-Dibromopyridine 626-55-1 696-40-2 768-35-4 1066-45-1, Trimethyltin chloride 1120-87-2 1121-22-8 1423-26-3 1436-59-5 1461-22-9, Tributyltin chloride 1489-69-6, Cyclopropanecarboxaldehyde 1556-18-9, Iodocyclopentane 1679-18-1 1696-17-9 1765-93-1 2156-04-9 2615-25-0 3218-36-8, [1,1'-Biphenyl]-4-carboxaldehyde 3385-21-5, 1,3 Cyclohexanediamine 3815-20-1, [1,1'-Biphenyl]-4-carboxamide 3900-89-8 3959-07-7, 4-Bromobenzylamine 4023-34-1, Cyclopropanoyl chloride 4530-20-5 5451-40-1 5720-05-8 5720-07-0 5856-63-3 6165-68-0 6165-69-1 6271-78-9 7144-05-0, 4-Piperidinemethanamine 10316-79-7 10365-98-7 13331-23-2 13331-27-6 14047-29-1 15761-38-3 17933-03-8 23138-64-9 24358-62-1 25487-66-5 27489-62-9 39546-32-2, 4-Piperidinecarboxamide 39684-80-5 50910-54-8 55499-43-9 55552-70-0 59020-10-9 63503-60-6 73918-56-6 78887-39-5 79286-79-6, 3-Pyrrolidinamine 85006-23-1 89878-14-8 98437-24-2 107099-99-0 115298-62-9 124252-41-1 144432-85-9 146552-71-8 162607-15-0 162607-18-3 162607-20-7 172975-69-8 269410-09-5
(preparation of biarylmethylaminopurines as potent cyclin/CDK inhibitors and antiproliferative agents)

IT 3385-21-5, 1,3 Cyclohexanediamine
(preparation of biarylmethylaminopurines as potent cyclin/CDK inhibitors and antiproliferative agents)

RN 3385-21-5 USPATFULL

CN 1,3-Cyclohexanediamine (CA INDEX NAME)



L79 ANSWER 26 OF 38 USPATFULL on STN

ACCESSION NUMBER: 2004:25216 USPATFULL Full-text

TITLE: Chemokine receptor binding heterocyclic compounds with enhanced efficacy

INVENTOR(S): Bridger, Gary, Bellingham, WA, UNITED STATES
Kaller, Al, Vancouver, CANADA
Harwig, Curtis, White Rock, CANADA
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Atsma, Bem, Abbotsford, CANADA
Nan, Siqiao, Richmond, CANADA
Zhou, Yuanxi, Surrey, CANADA
Schols, Dominique, Herent, BELGIUM
Smith, Christopher D., Vancouver, CANADA
Di Fluri, Maria R., Burnaby, CANADA

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004019058	A1	20040129	
APPLICATION INFO.:	US 2003-457034	A1	20030606 (10)	<--

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-446170, filed on 23 May 2003, PENDING Continuation-in-part of Ser. No. US 2002-329329, filed on 23 Dec 2002, PENDING

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2001-342716P	20011221 (60)	<--
	US 2002-350822P	20020117 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Kate H. Murashige, Morrison & Foerster LLP, Suite 500, 3811 Valley Centre Drive, San Diego, CA, 92130-2332
NUMBER OF CLAIMS: 50
EXEMPLARY CLAIM: 1
LINE COUNT: 13653

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to heterocyclic compounds consisting of a core nitrogen atom surrounded by three pendant groups, wherein two of the three pendant groups are preferably benzimidazolyl methyl and tetrahydroquinolyl, and the third pendant group contains N and optionally contains additional rings. The compounds bind to chemokine receptors, including CXCR4 and CCR5, and demonstrate protective effects against infection of target cells by a human immunodeficiency virus (HIV).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . pH, the compounds of the invention will be in the forms of the acid addition salts. Particularly preferred are the hydrochlorides. In addition, when prepared as purified forms, the compounds may also be crystallized as the hydrates.

DETD [0133] To a stirred solution of (2-aminomethyl)benzimidazole dihydrochloride hydrate (5.96 g, 27.1 mmol) in dry MeOH (225 mL) was added 6,7-dihydro-5H-quinolin-8-one (3.99 g, 27.1 mmol) and the mixture. . .

DETD [0259] Compound 18: Preparation of N'-(1H-benzimidazol-2-ylmethyl)-N'-(S)-5,6,7,8-tetrahydro-quinolin-8-yl-butane-1,4-diamine (Hydrochloride Salt).

DETD . . . General Procedure B: To a stirred solution of 4-[(1H-Benzoimidazole-2-ylmethyl)-(5,6,7,8-tetrahydro-quinolin-8-yl)-amino]-butyraldehyde (see COMPOUND 32 for preparation) (0.2182 g, 0.63 mmol) and aminoguanadine hydrochloride (69 mg, 0.63 mmol) in dry MeOH

(4 mL) was added AcOH (75 μL, 1.26 mmol) and the mixture was. . .

DETD [0309] A solution of N.sup.1-(5,6,7,8-tetrahydro-quinolin-8-yl)-N-[1-(2-trimethylsilanyl-ethoxymethyl)-1H-benzoimidazol-2-ylmethyl]-butane-1,4-diamine (170 mg, 0.35 mmol), 1-H-pyrazole-1-carboxamidine hydrochloride (51 mg, 0.35 mmol) and DIPEA (61 μL, 0.35 mmol) in THF (0.2 mL) was stirred at room temperature for. . .

DETD [0349] To a stirred solution of 4-(methylamino)-butyric acid hydrochloride (303 mg, 1.97 mmol) and dioxane (2 mL) in saturated aqueous NaHCO.sub.3 (2 mL) was added added di-tert-butyl di-carbonate (523. . .

DETD [0450] Compound 44: Preparation of (trans-2-aminomethyl-cyclopropylmethyl)-(1H-benzimidazol-2-ylmethyl)-(S)-5,6,7,8-tetrahydroquinlin-8-yl-amine (hydrochloride salt).

DETD [0465] Preparation of (trans-2-aminomethyl-cyclopropylmethyl)-(1H-benz-imidazol-2-ylmethyl)-(S)-5,6,7,8-tetrahydroquinlin-8-yl-amine (Hydrochloride Salt) (Compound 44):

DETD . . . To a solution of the crude aldehyde from above (90 mg, 0.17 mmol) in methanol (1.5 mL) was added hydroxyamine hydrochloride salt (23 mg, 0.33 mmol) and the mixture was stirred at room temperature for 40 minutes. The mixture was concentrated. . .

DETD [0556] A solution of trans-4-aminocyclohexanol hydrochloride (2.67 g, 1.14 mol) in 1 N NaOH (40 mL) was washed with CHCl.sub.3 (40 mL), CH.sub.2Cl.sub.2 (2×30 mL) and. . .

DETD [0570] Compound 55: Preparation of N.sup.1-(1H-Benzimidazol-2-ylmethyl)-N.sup.1-((S)-5,6,7,8-tetrahydro-quinolin-8-yl)-trans-cyclohexane-14-diamine (Hydrochloride Salt)

DETD [0571] To a solution of trans-4-aminocyclohexanol hydrochloride (10.0 g, 65.9 mmol) and triethylamine (18.4 mL, 132.0 mmol) in tetrahydrofuran (132 mL) was added di-tert-butyl dicarbonate (15.31 g,. . .

DETD [0709] To a stirred suspension of (Z)-4-chloro-2-butenylamine hydrochloride (1.0 g, 7.0 mmol) in THF (35 mL) and water (0.2 mL) was added N,N-diisopropylethylamine (2.7 mL, 15.4 mmol) followed. . .

DETD [0717] Compound 76: Preparation of (Z)--N.sup.1-(1H-Benzimidazol-2-ylmethyl)-N.sup.1-5.6,7,8-tetrahydro-quinolin-8-yl-but-2-ene-1,4-diamine (Hydrochloride Salt)

DETD [0718] (Z)-4-chloro-2-butenylamine hydrochloride (3.88 g, 27.3 mmol), water (1 mL) and diisopropylethylamine (9.6 mL, 55.1 mmol) were dissolved in tetrahydrofuran (140 mL) and. . .

DETD [0730] To a stirred mixture of 1-amino-4-chloro-2-butyne hydrochloride (1.12 g, 8.01 mmol) and Boc.sub.2O (2.12 g, 9.71 mmol) in a solution of THF (40 mL) and H.sub.2O (15. . .

DETD [0771] A solution of trans-2-aminocyclohexanol hydrochloride (1.185 g, 7.81 mmol) and 2-nitrobenzenesulfonyl chloride (1.73 g, 7.81 mmol) in CH.sub.2Cl.sub.2 (20 mL) was cooled in an ice. . .

DETD . . . was then washed with diethyl ether (3×20 mL) and dried in vacuo. This afforded the required 4-[(1H-benzimidazol-2-ylmethyl)-(5,6,7,8-tetrahydroquinolin-8-yl)-amino]-butyrimidic acid methyl ester (hydrochloride salt), which was used immediately in the next reaction.

DETD [0884] To a solution of (1-H-benzimidazol-2-ylmethyl)-(5,6,7,8-tetrahydro-quinolin-8-yl)-(1-(N-phthalimidyl)-butan-2-one-4-yl)-amine (58 mg, 0.117 mmol) in methanol (5 mL) was added hydroxylamine hydrochloride (83.5 mg, 1.0 mmol). The resulting solution was stirred at room temperature overnight. Aqueous sodium bicarbonate (5 mL of a. . .

DETD . . . mmol). The resulting suspension was stirred for 10 minutes, then a solution of 3-nitroanisole (1.55 g, 10.1 mmol) and methoxylamine hydrochloride (1.08 g, 12.9 mmol) in DMF (15 mL) was added in a dropwise manner over 15 minutes. The mixture was. . .

DETD [0939] Compound 102: Preparation of N.sup.1-(1-Methyl-1H-benzoimidazol-2-

ylmethyl)-N.sup.1-(S)-(5,6,7,8-tetrahydro-quinolin-8-yl)-butane-1,4-diamine Hydrochloride Salt

DETD [0986] Compound 107: Preparation of N.sup.1-(1H-Benzimidazol-2-ylmethyl)-N.sup.1-(S)-3,4-dihydro-2H-[3,2-b]pyridin-4-yl-butane-1,4-diamine (Hydrochloride Salt).

DETD [0993] A solution of the ketone (2.9 g, 19 mmol) from above and hydroxylamine hydrochloride (1.6 g, 23 mmol) in methanol (100 mL) was stirred at room temperature for 1 h. Saturated sodium bicarbonate solution. . .

DETD [0996] Preparation of N.sup.1-(1H-Benzimidazol-2-ylmethyl)-N.sup.1-(S)-3,4-dihydo-2H-pyrano[3,2-b]pyridin-4-yl-butane-1,4-diamine Hydrochloride Salt (Compound 107):

DETD [1000] Following General Procedure D: Conversion of the free base (1.80 g, 5.1 mmol) from above to the hydrochloride salt gave COMPOUND 107 (2.14 g, 82%) as a white solid. .sup.1H NMR (D.sub.2O) δ 1.49-1.60 (m, 4H), 2.39-2.49 (m,. . .

DETD [1051] Compound 114: Preparation of N.sup.1-(4-Methoxy-1H-benzoindiazol-2-ylmethyl)-N.sup.1-(S)-(5,6,7,8-tetrahydro-quinolin-8-yl)-butane-1,4-diamine) Hydrochloride Salt)

DETD [1128] Compound 123: Preparation of N.sup.1-(1-Allyl-1H-benzimidazol-2-ylmethyl)-N.sup.1-(S)-5.6,7,8-tetrahydro-quinolin-8-yl-butane-1,4-diamine (Hydrochloride Salt)

DETD [1240] To absolution of 4-(hydroxymethyl)imidazole hydrochloride (578 mg, 4.30 mmol) in DMF (3.5 mL) was added DIPEA (1.9 mL, 10.9 mmol) and 2-(trimethylsilyl)ethoxymethyl chloride (0.83 mL,. . .

DETD [1248] Compound 135: Preparation of N.sup.1-(1-Allyl-1H-imidazol-2-ylmethyl)-N.sup.1-(S)-5,6,7,8-tetrahydro-quinolin-8-yl-butane-1,4-diamine (Hydrochloride Salt)

DETD [1254] Following general procedure D, conversion of the material to his hydrochloride salt and re-precipitation from methanol/diethylether gave COMPOUND 135 (7.97 g, 82%) as beige solid. .sup.1H NMR (300 MHz, D.sub.2O, δ. . .

DETD . . . the above amine (173 mg, 0.52 mmol) in DMF (3 mL) was added 1-hydroxybenzotriazole hydrate (104 mg, 0.77 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (148 mg, 0.77 mmol), and 6-hydroxynicotinic acid (86 mg, 0.62 mmol). The reaction was stirred overnight at room temperature. Then. . .

DETD . . . solution of N.sup.1-(1H-benzoimidazol-2-ylmethyl)-N.sup.1-(5,6,7,8-tetrahydro-quinolin-8-yl)-propane-1,3-diamine (166 mg, 0.50 mmol) in DMF (3 mL) was added 1-hydroxybenzotriazole hydrate (100 mg, 0.74 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (142 mg, 0.74 mmol), and benzoic acid (73 mg, 0.59 mmol). The reaction mixture was stirred overnight at room temperature.. . .

DETD . . . of 5-bromonicotinic acid (120 mg, 0.60 mmol) in DMF (3 mL) was added 1-hydroxybenzotriazole hydrate (96 mg, 0.72 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (137 mg, 0.72 mmol), N,N-diisopropylethylamine (0.21 mL, 1.19 mmol), and N.sup.1-(1H-benzoimidazol-2-ylmethyl)-N.sup.1-(5,6,7,8-tetrahydro-quinolin-8-yl)-propane-1,3-diamine (200 mg, 0.60 mmol). The reaction mixture was stirred. . .

DETD . . . of cinnoline-4-carboxylic acid (80 mg, 0.46 mmol) in DMF (3 mL) was added 1-hydroxybenzotriazole hydrate (74 mg, 0.55 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (106 mg, 0.55 mmol), N,N-diisopropylethylamine (0.16 mL, 0.92 mmol), and N"-(1H-benzoimidazol-2-ylmethyl)-N.sup.1-(5,6,7,8-tetrahydro-quinolin-8-yl)-propane-1,3-diamine (154 mg, 0.46 mmol). The reaction mixture was stirred. . .

DETD [1346] 4-[(1-Allyl-1H-benzoimidazol-2-ylmethyl)-(5,6,7,8-tetrahydro-quinolin-8-yl)-amino]-butyl hydrochloride salt (120 mg, 0.215 mmol)

was neutralized with 1M NaOH (25 mL) and the free base was extracted with CHCl.sub.3. . .

DETD [1353] N.sup.1-(1-Allyl-1H-imidazol-2-ylmethyl)-N.sup.1-(S)-5,6,7,8-tetrahydro-quinolin-8-yl-butane-1,4-diamine, Hydrochloride salt (115.1 mg, 0.216 mmol) was neutralized with 1M NaOH (25 mL) and the free base was extracted with CHCl.sub.3. . .

DETD [1356] Compound 157: Preparation of (Cis-2-Aminomethyl-cylcopropylmethyl)-(1H-benzimidazol-2-ylmethyl)-(S)-5,6,7,8-tetrahydro-quinolin-8-yl-amine (Hydrochloride Salt).

DETD [1365] Preparation of (Cis-2-Aminomethyl-cylcopropylmethyl)-(1H-benzimidazol-2-ylmethyl)-(S)-5,6,7,8-tetrahydro-quinolin-8-yl-amine (hydrochloride salt) (Compound 157):

DETD [1368] Following General Procedure D: Conversion of the free base (2.80 g, 7.7 mmol) from above to the hydrochloride salt provided COMPOUND 157 (3.30 g, 87%) as a white solid. .sup.1H NMR (D.sub.2O) δ 0.08 (q, 1H, J=5.0 Hz),. . .

DETD [1374] ((1R,2S)-2-Aminomethyl-cylcopropylmethyl)-(1H-benzimidazol-2-ylmethyl)-(S)-5,6,7,8-tetrahydro-quinolin-8-yl-amine, hydrochloride salt (107.2 mg, 0.217 mmol) was neutralized with 1M NaOH (25 mL) and the free base was extracted with CHCl.sub.3. . .

DETD [1380] 3-Aminomethyl-N-(1H-benzoimidazol-2-ylmethyl)-N-(5,6,7,8-tetrahydro-quinolin-8-yl)-but-2-ene-1,4-diamine, Hydrochloride salt (213.8 mg, 0.365 mmol) was neutralized with 1M NaOH (25 mL) and the free base was extracted with CHCl.sub.3. . .

DETD [1384] Compound 160: 3-Aminomethyl-N.sup.1-(1H-benzoimidazol-2-ylmethyl)-N--(S)-(5,6,7,8-tetrahydro-quinolin-8-yl)-but-2-ene-14-diamine Hydrochloride Salt

DETD [1458] Preparation of Carbonic Acid pyrrolidin-3-ylmethyl Ester Vinyl Ester Hydrochloride: ##STR213##

DETD . . . was added THF (4 mL), Et.sub.3N (0.58 mL, 4.2 mmol), and a solution of carbonic acid pyrrolidin-3-ylmethyl ester vinyl ester hydrochloride (284 mg, 1.37 mmol) in THF (3 mL), and the mixture was stirred at room temperature for 21 h. The. . .

IT 65-85-0, Benzoic acid, reactions 75-31-0, Isopropylamine, reactions 79-33-4, L-Lactic acid, reactions 93-10-7, Quinoline-2-carboxylic acid 93-53-8, 2-Phenylpropionaldehyde 93-97-0, Benzoic anhydride 95-54-5, 1,2-Phenylenediamine, reactions 96-32-2, Methyl bromoacetate 98-97-5, 2-Pyrazinecarboxylic acid 98-98-6, Picolinic acid 100-46-9, Benzylamine, reactions 100-52-7, Benzaldehyde, reactions 100-58-3, Phenylmagnesium bromide 104-98-3, Urocanic acid 105-36-2, Ethyl bromoacetate 106-95-6, Allyl bromide, reactions 107-11-9, Allylamine 107-18-6, Allyl alcohol, reactions 110-63-4, 1,4-Butanediol, reactions 110-91-8, Morpholine, reactions 123-72-8, Butyraldehyde 124-02-7, Diallylamine 156-87-6, 3-Amino-1-propanol 273-21-2, 4-Azabenzimidazole 288-32-4, Imidazole, reactions 487-89-8, Indole-3-carboxaldehyde 504-02-9, 1,3-Cyclohexanedione 555-03-3, 3-Nitroanisole 592-57-4, 1,3-Cyclohexadiene 603-35-0, Triphenylphosphine, reactions 609-65-4, 2-Chlorobenzoyl chloride 616-29-5, 1,3-Diamino-2-hydroxypropane 616-30-8, 3-Amino-1,2-propanediol 617-52-7, Dimethyl itaconate 623-27-8, 1,4-Benzenedicarboxaldehyde 627-27-0, 3-Buten-1-ol 765-30-0, Cyclopropylamine 822-36-6, 4-Methylimidazole 826-34-6, Dimethyl cis-1,2-cyclopropanedicarboxylate 867-13-0, Triethyl phosphonoacetate 1074-82-4, Potassium phthalimide 1099-45-2, (Carbethoxymethylene)triphenylphosphorane 1121-60-4, Pyridine-2-carboxaldehyde 1126-09-6, Ethyl isonipecotate 1477-50-5, Indole-2-carboxylic acid 1694-92-4, 2-Nitrobenzenesulfonyl chloride 2605-67-6, Methyl (triphenylphosphoranylidene)acetate 2615-25-0, trans-1,4-Cyclohexanediamine 2859-68-9, 3-(2-Pyridyl)-1-propanol 3012-80-4, 1-Methyl-1H-benzimidazole-2-carboxaldehyde 3385-21-5

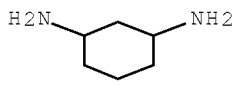
, 1,3-Cyclohexanediamine 3433-37-2, 2-Piperidinemethanol 3752-24-7, 4,5,6,7-Tetrahydro-1H-benzimidazole 3920-50-1, Pyrazole-3-carboxaldehyde 3999-55-1, Diethyl trans-1,2-cyclopropanedicarboxylate 4023-02-3, 1H-Pyrazole-1-carboxamidine hydrochloride 4048-33-3, 6-Amino-1-hexanol 4606-65-9, 3-Piperidinemethanol 4760-34-3, N-Methyl-o-phenylenediamine 4856-97-7, 2-Hydroxymethylbenzimidazole 5006-66-6, 6-Hydroxynicotinic acid 5130-24-5, Vinyl chloroformate 5332-06-9, 4-Bromobutyronitrile 5332-24-1, 3-Bromoquinoline 5382-16-1, 4-Hydroxypiperidine 5414-21-1, 5-Bromovaleronitrile 5456-63-3, trans-2-Aminocyclohexanol hydrochloride 5731-17-9, (1-Benzylpyrrolidin-3-yl)methanol 5993-91-9, 2-(Aminomethyl)benzimidazole dihydrochloride 6602-32-0, 2-Bromo-3-pyridinol 6624-49-3, 3-Isoquinolinecarboxylic acid 6859-99-0, 3-Hydroxypiperidine 6976-17-6, 4-(Methylamino)butyric acid hydrochloride 7051-34-5, (Bromomethyl)cyclopropane 7153-66-4, (Z)-4-Chloro-2-butenylamine hydrochloride 7197-96-8, 2,3-Cycloheptenopyridine 10111-08-7, Imidazole-2-carboxaldehyde 13325-10-5, 4-Amino-1-butanol 13750-81-7, 1-Methyl-2-imidazolecarboxaldehyde 13958-93-5, 3,5-Dichloroisonicotinic acid 14080-23-0, 2-Cyanopyrimidine 14631-46-0, 8-Hydroxy-5,6,7,8-tetrahydroquinoline 16139-18-7, Aminoguanidine hydrochloride 20826-04-4, 5-Bromonicotinic acid 21905-86-2, Cinnoline-4-carboxylic acid 22059-21-8, 1-Aminocyclopropanecarboxylic acid 26690-80-2, (2-Hydroxyethyl)carbamic acid tert-butyl ester 29602-39-9, 2-[(2-Aminoethyl)amino]-5-nitropyridine 31106-82-8, 2-(Bromomethyl)pyridine hydrobromide 32673-41-9, 4-(Hydroxymethyl)imidazole hydrochloride 33036-62-3, 4-Bromobutan-1-ol 34413-35-9, 5,6,7,8-Tetrahydroquinoxaline 38666-30-7, 5,6,7,8-Tetrahydroimidazo[1,5-a]pyridine 42383-61-9, 2-Aminoimidazole sulfate 46153-01-9, 2-Methyl-5,6-dihydro-4H-imidazo[4,5,1-ij]quinoline 50910-54-8, trans-4-Aminocyclohexanol hydrochloride 53054-03-8, (2S)-5-Amino-2-(tert-butoxycarbonylamino)pentanoic acid tert-butyl ester 58885-58-8, (3-Hydroxypropyl)carbamic acid tert-butyl ester 61388-89-4, 2-Methyl-8-acetamidoquinoline 66715-65-9, 2-Pyridinesulfonyl chloride 68076-36-8, (4-Aminobutyl)carbamic acid tert-butyl ester 69610-41-9, N-(tert-Butoxycarbonyl)-L-prolinal 72998-92-6, 2-Chloromethyl-5,6-dimethyl-1H-benzimidazole 76513-69-4, [2-(Trimethylsilyl)ethoxy]methyl chloride 77369-59-6, 1-Amino-4-chloro-2-butyne hydrochloride 80567-69-7, 2-Chloromethyl-4-methyl-1H-benzimidazole 102089-74-7, (R)-N-(tert-Butoxycarbonyl)-2-phenylglycinol 104249-15-2, N-((E)-4-Bromo-2-butenyl)phthalimide 107430-29-5, 2-Chloromethyl-6-trifluoromethyl-1H-benzimidazole 117049-14-6, (S)-N-(tert-Butoxycarbonyl)-2-phenylglycinol 125163-05-5, 8-Hydroxy-4-methoxy-5,6,7,8-tetrahydroquinoline 130861-73-3, 2-Chloro-8-hydroxy-5,6,7,8-tetrahydroquinoline 156144-42-2, 2-Chloromethyl-5-fluoro-1H-benzimidazole 157634-00-9, 2-Hydroxymethylpiperidine-1-carboxylic acid tert-butyl ester 163798-87-6, 1-(tert-Butoxycarbonyl)-2-chloromethylbenzimidazole 229328-97-6, 3,5-Dichloroisonicotinoyl chloride 298181-83-6, 8-Amino-5,6,7,8-tetrahydroquinoline 369655-84-5, ((R)-5,6,7,8-Tetrahydroquinolin-8-yl)amine 369656-57-5, (S)-5,6,7,8-Tetrahydroquinolin-8-ylamine 405173-68-4, 2-Chloromethyl-4,5-dimethyl-1H-benzimidazole 405173-94-6, 2-Chloromethyl-7-fluoro-1H-benzimidazole 405174-39-2, 4-(4-Fluorophenyl)-1-[(2-trimethylsilanylethoxy)methyl]-1H-imidazole-2-carboxaldehyde 507228-47-9, [tert-Butoxycarbonylimino(4-oxopiperidin-1-yl)methyl]carbamic acid tert-butyl ester 558441-93-3, 4-[(1H-Benzimidazole-2-ylmethyl)(5,6,7,8-tetrahydroquinolin-8-yl)amino]butyraldehyde 558442-56-1, [[1-(tert-Butoxycarbonyl)benzimidazol-2-yl]methyl](5,6,7,8-tetrahydroquinolin-8-yl)[(4S)-4-phenyl-4-(tert-butoxycarbonylamino)butyl]amine 558442-84-5,

N1-(1H-Benzimidazol-2-ylmethyl)-N1-(5,6,7,8-tetrahydroquinolin-8-yl)-N4-benzylcyclohexane-trans-1,4-diamine 558443-56-4, [[1-(tert-Butoxycarbonyl)-1H-benzimidazol-2-yl]methyl](5,6,7,8-tetrahydroquinolin-8-yl)(3-cyanopropyl)amine 558443-80-4, 2-[4-(tert-Butyldimethylsilanyloxy)-2-hydroxybutyl]isoindole-1,3-dione 558444-72-7, 2-[4-[((S)-5,6,7,8-Tetrahydroquinolin-8-yl)amino]butyl]isoindole-1,3-dione 558445-48-0, 2-Chloromethyl-4-methoxybenzimidazole-1-carboxylic acid tert-butyl ester 558446-25-6, N-(5,6,7,8-Tetrahydroquinolin-8-yl)butane-1,4-diamine 558447-10-2, N'-((S)-5,6,7,8-Tetrahydroquinolin-8-yl)butane-1,4-diamine 558447-26-0, N'-(1H-Benzimidazol-2-ylmethyl)-N'-((S)-5,6,7,8-tetrahydroquinolin-8-yl)butane-1,4-diamine 558447-80-6, 4-[[(1-Allyl-1H-benzimidazol-2-yl)methyl]((S)-5,6,7,8-tetrahydroquinolin-8-yl)amino]butylamine hydrochloride 558447-89-5, (1H-Benzimidazol-2-ylmethyl)((S)-5,6,7,8-tetrahydroquinolin-8-yl)amine 558447-98-6, 3-Aminomethyl-N-(1H-benzimidazol-2-ylmethyl)-N-(5,6,7,8-tetrahydroquinolin-8-yl)but-2-ene-1,4-diamine hydrochloride
(preparation of chemokine receptor binding benzimidazolylmethyl tetrahydroquinolinyl amines and related heterocyclic compds. with enhanced efficacy against AIDS and other disorders)

IT 3385-21-5, 1,3-Cyclohexanediamine
(preparation of chemokine receptor binding benzimidazolylmethyl tetrahydroquinolinyl amines and related heterocyclic compds. with enhanced efficacy against AIDS and other disorders)

RN 3385-21-5 USPATFULL

CN 1,3-Cyclohexanediamine (CA INDEX NAME)



L79 ANSWER 27 OF 38 USPATFULL on STN

ACCESSION NUMBER: 2003:312736 USPATFULL Full-text

TITLE: Chemokine receptor binding heterocyclic compounds with enhanced efficacy

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PATENT INFORMATION:	US 2003220341	A1	20031127		<--
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FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	Kate H. Murashige, Morrison & Foerster LLP, Suite 500, 3811 Valley Centre Drive, San Diego, CA, 92130-2332		
NUMBER OF CLAIMS:	39		
EXEMPLARY CLAIM:	1		
LINE COUNT:	13158		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to heterocyclic compounds consisting of a core nitrogen atom surrounded by three pendant groups, wherein two of the three pendant groups are preferably benzimidazolyl methyl and tetrahydroquinolyl, and the third pendant group contains N and optionally contains additional rings. The compounds bind to chemokine receptors, including CXCR4 and CCR5, and demonstrate protective effects against infection of target cells by a human immunodeficiency virus (HIV).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD [0118] To a stirred solution of (2-aminomethyl)benzimidazole dihydrochloride hydrate (5.96 g, 27.1 mmol) in dry MeOH (225 mL) was added 6,7-dihydro-5H-quinolin-8-one (3.99 g, 27.1 mmol) and the mixture. . .

DETD [0244] COMPOUND 18: Preparation of N'-(1H-benzimidazol-2-ylmethyl)-N'-(S)-5,6,7,8-tetrahydro-quinolin-8-yl-butane-1,4-diamine (Hydrochloride Salt).

DETD . . . General Procedure B: To a stirred solution of 4-[(1H-Benzoimidazole-2-ylmethyl)-(5,6,7,8-tetrahydro-quinolin-8-yl)-amino]-butyraldehyde (see COMPOUND 32 for preparation) (0.2182 g, 0.63 mmol) and aminoguanadine hydrochloride (69 mg, 0.63 mmol) in dry MeOH (4 mL) was added AcOH (75 μL, 1.26 mmol) and the mixture was. . .

DETD [0295] A solution of N.sup.1-(5,6,7,8-tetrahydro-quinolin-8-yl)-N'-[1-(2-trimethylsilanyl-ethoxymethyl)-1H-benzoimidazol-2-ylmethyl]-butane-1,4-diamine (170 mg, 0.35 mmol), 1-H-pyrazole-1-carboxamidine hydrochloride (51 mg, 0.35 mmol) and DIPEA (61 μL, 0.35 mmol) in THF (0.2 mL) was stirred at room temperature for. . .

DETD [0335] To a stirred solution of 4-(methylamino)-butyric acid hydrochloride (303 mg, 1.97 mmol) and dioxane (2 mL) in saturated aqueous NaHCO.sub.3 (2 mL) was added added di-tert-butyl di-carbonate (523. . .

DETD [0435] COMPOUND 44: Preparation of (trans-2-aminomethyl-cyclopropylmethyl)-(1H-benz-imidazol-2-ylmethyl)-(S)-5,6,7,8-tetrahydroquinlin-8-yl-amine (Hydrochloride Salt).

DETD [0450] Preparation of (trans-2-aminomethyl-cyclopropylmethyl)-(1H-benz-imidazol-2-ylmethyl)-(S)-5,6,7,8-tetrahydroquinlin-8-yl-amine (Hydrochloride Salt)

DETD . . . To a solution of the crude aldehyde from above (90 mg, 0.17 mmol) in methanol (1.5 mL) was added hydroxyamine hydrochloride salt (23 mg, 0.33 mmol) and the mixture was stirred at room temperature for 40 minutes. The mixture was concentrated. . .

DETD [0542] A solution of trans-4-aminocyclohexanol hydrochloride (2.67 g, 1.14 mol) in 1 N NaOH (40 mL) was washed with CHCl.sub.3 (40 mL), CH.sub.2Cl.sub.2 (2×30 mL) and. . .

DETD [0556] COMPOUND 55: Preparation of N.sup.1-(1H-Benzimidazol-2-ylmethyl)-N'-((S)-5,6,7,8-tetrahydro-quinolin-8-yl)-trans-cyclohexane-1,4-diamine (Hydrochloride Salt)

DETD [0557] To a solution of trans-4-aminocyclohexanol hydrochloride (10.0 g, 65.9 mmol) and triethylamine (18.4 mL, 132.0 mmol) in tetrahydrofuran (132 mL) was added di-tert-butyl dicarbonate (15.31 g,. . .

DETD [0696] To a stirred suspension of (Z)-4-chloro-2-butenylamine hydrochloride (1.0 g, 7.0 mmol) in THF (35 mL) and water (0.2 mL) was added N,N-diisopropylethylamine (2.7 mL, 15.4 mmol) followed. . .

DETD [0704] COMPOUND 76: Preparation of (Z)-N.sup.1-(1H-Benzimidazol-2-ylmethyl)-N.sup.1-5,6,7,8-tetrahydro-quinolin-8-yl-but-2-ene-1.4-diamine (Hydrochloride Salt)

DETD [0705] (Z)-4-chloro-2-butenylamine hydrochloride (3.88 g, 27.3 mmol), water (1 mL) and diisopropylethylamine (9.6 mL, 55.1 mmol) were dissolved in tetrahydrofuran (140 mL) and. . .

DETD [0717] To a stirred mixture of 1-amino-4-chloro-2-butyne hydrochloride (1.12 g, 8.01 mmol) and Boc.sub.2O (2.12 g, 9.71 mmol) in a solution of THF (40 mL) and H.sub.2O (15. . .

DETD [0758] A solution of trans-2-aminocyclohexanol hydrochloride (1.185 g, 7.81 mmol) and 2-nitrobenzenesulfonyl chloride (1.73 g, 7.81 mmol) in CH.sub.2Cl.sub.2 (20 mL) was cooled in an ice. . .

DETD . . . was then washed with diethyl ether (3×20 mL) and dried in vacuo. This afforded the required 4-[(1H-benzimidazol-2-ylmethyl)-(5,6,7,8-tetrahydroquinolin-8-yl)-amino]-butyrimidic acid methyl ester (Hydrochloride salt), which was used immediately in the next reaction.

DETD [0871] To a solution of (1-H-benzimidazol-2-ylmethyl)-(5,6,7,8-tetrahydro-quinolin-8-yl)-(1-(N-phthalimidyl)-butan-2-one-4-yl)-amine (58 mg, 0.117 mmol) in methanol (5 mL) was added hydroxylamine hydrochloride (83.5 mg, 1.0 mmol). The resulting solution was stirred at room temperature overnight. Aqueous sodium bicarbonate (5 mL of a. . .

DETD . . . mmol). The resulting suspension was stirred for 10 minutes, then a solution of 3-nitroanisole (1.55 g, 10.1 mmol) and methoxylamine hydrochloride (1.08 g, 12.9 mmol) in DMF (15 mL) was added in a dropwise manner over 15 minutes. The mixture was. . .

DETD [0925] COMPOUND 102: Preparation of N.sup.1-(1-Methyl-1H-benzoimidazol-2-ylmethyl)-N.sup.1-(S)-(5,6,7,8-tetrahydro-quinolin-8-yl)-butane-1,4-diamine Hydrochloride Salt

DETD [0972] COMPOUND 107: Preparation of N.sup.1-(1H-Benzimidazol-2-ylmethyl)-N.sup.1--(S)-3,4-dihydro-2H-pyrano[3,2-b]pyridin-4-yl-butane-1,4-diamine (Hydrochloride Salt).

DETD [0979] A solution of the ketone (2.9 g, 19 mmol) from above and hydroxylamine hydrochloride (1.6 g, 23 mmol) in methanol (100 mL) was stirred at room temperature for 1 h. Saturated sodium bicarbonate solution. . .

DETD [0982] Preparation of N.sup.1-(1H-Benzimidazol-2-ylmethyl)-N.sup.1-(S)-3,4-dihydo-2H-pyrano[3,2-b]pyridin-4-yl-butane-1,4-diamine Hydrochloride Salt (COMPOUND 107):

DETD [0986] Following General Procedure D: Conversion of the free base (1.80 g, 5.1 mmol) from above to the hydrochloride salt gave COMPOUND 107 (2.14 g, 82%) as a white solid. .sup.1H NMR (D.sub.2O) δ 1.49-1.60 (m, 4H), 2.39-2.49 (m,. . .

DETD [1040] COMPOUND 114: Preparation of N.sup.1-(4-Methoxy-1H-benzoindiazol-2-ylmethyl)-N.sup.1-(S)-(5.6,7,8-tetrahydro-quinolin-8-yl)-butane-1,4-diamine)Hydrochloride Salt)

DETD [1117] COMPOUND 123: Preparation of N.sup.1-(1-Allyl-1H-benzimidazol-2-ylmethyl)-N.sup.1-(S)-5,6,7,8-tetrahydro-quinolin-8-yl-butane-1,4-diamine (Hydrochloride Salt)

DETD [1227] To a solution of 4-(hydroxymethyl)imidazole hydrochloride (578 mg, 4.30 mmol) in DMF (3.5 mL) was added DIPEA (1.9 mL, 10.9 mmol) and 2-(trimethylsilyl)ethoxymethyl chloride (0.83 mL,. . .

DETD [1235] COMPOUND 135: Preparation of N.sup.1-(1-Allyl-1H-imidazol-2-ylmethyl)-N.sup.1-(S)-5,6,7,8-tetrahydro-quinolin-8-yl-butane-1,4-

diamine (Hydrochloride Salt)

DETD [1241] Following general procedure D, conversion of the material to his hydrochloride salt and re-precipitation from methanol/diethylether gave COMPOUND 135 (7.97 g, 82%) as beige solid. .sup.1H NMR (300 MHz, D.sub.2O, 6. . .

DETD . . . the above amine (173 mg, 0.52 mmol) in DMF (3 mL) was added 1-hydroxybenzotriazole hydrate (104 mg, 0.77 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (148 mg, 0.77 mmol), and 6-hydroxynicotinic acid (86 mg, 0.62 mmol). The reaction was stirred overnight at room temperature. Then. . .

DETD . . . solution of N.sup.1-(1H-benzoimidazol-2-ylmethyl)-N-(5,6,7,8-tetrahydro-quinolin-8-yl)-propane-1,3-diamine (166 mg, 0.50 mmol) in DMF (3 mL) was added 1-hydroxybenzotriazole hydrate (100 mg, 0.74 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarboduimide hydrochloride (142 mg, 0.74 mmol), and benzoic acid (73 mg, 0.59 mmol). The reaction mixture was stirred overnight at room temperature.. . .

DETD . . . of 5-bromonicotinic acid (120 mg, 0.60 mmol) in DMF (3 mL) was added 1-hydroxybenzotriazole hydrate (96 mg, 0.72 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (137 mg, 0.72 mmol), N,N-diisopropylethylamine (0.21 mL, 1.19 mmol), and N.sup.1-(1H-benzoimidazol-2-ylmethyl)-N'-(5,6,7,8-tetrahydro-quinolin-8-yl)-propane-1,3-diamine (200 mg, 0.60 mmol). The reaction mixture was stirred. . .

DETD . . . of cinnoline-4-carboxylic acid (80 mg, 0.46 mmol) in DMF (3 mL) was added 1-hydroxybenzotriazole hydrate (74 mg, 0.55 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (106 mg, 0.55 mmol), N,N-diisopropylethylamine (0.16 mL, 0.92 mmol), and N.sup.1-(1H-benzoimidazol-2-ylmethyl)-N.sup.1-(5,6,7,8-tetrahydro-quinolin-8-yl)-propane-1,3-diamine (154 mg, 0.46 mmol). The reaction mixture was stirred. . .

DETD [1333] 4-[(1-Allyl-1H-benzoimidazol-2-ylmethyl)-(5,6,7,8-tetrahydro-quinolin-8-yl)-amino]-butyl hydrochloride salt (120 mg, 0.215 mmol) was neutralized with 1M NaOH (25 mL) and the free base was extracted with CHCl.sub.3. . .

DETD [1340] N.sup.1-(1-Allyl-1H-imidazol-2-ylmethyl)-NM-(S)-5,6,7,8-tetrahydro-quinolin-8-yl-butane-1,4-diamine, Hydrochloride salt (115.1 mg, 0.216 mmol) was neutralized with 1M NaOH (25 mL) and the free base was extracted with CHCl.sub.3. . .

DETD [1343] COMPOUND 157: Preparation of (Cis-2-Aminomethyl-cylcopropylmethyl)-(1H-benzimidazol-2-ylmethyl)-(S)-5,6,7,8-tetrahydro-quinolin-8-yl-amine (Hydrochloride Salt).

DETD [1352] Preparation of (Cis-2-Aminomethyl-cylcopropylmethyl)-(1H-benzimidazol-2-ylmethyl)-(S)-5,6,7,8-tetrahydro-quinolin-8-yl-amine (Hydrochloride Salt)

DETD [1356] Following General Procedure D: Conversion of the free base (2.80 g, 7.7 mmol) from above to the hydrochloride salt provided COMPOUND 157 (3.30 g, 87%) as a white solid. .sup.1H NMR (D.sub.2O) δ 0.08 (q, 1H, J=5.0 Hz),. . .

DETD [1362] ((1R,2S)-2-Aminomethyl-cylcopropylmethyl)-(1H-benzimidazol-2-ylmethyl)-(S)-5,6,7,8-tetrahydro-quinolin-8-yl-amine, hydrochloride salt (107.2 mg, 0.217 mmol) was neutralized with 1M NaOH (25 mL) and the free base was extracted with CHCl.sub.3. . .

DETD [1368] 3-Aminomethyl-N-(1H-benzoimidazol-2-ylmethyl)-N-(5,6,7,8-tetrahydro-quinolin-8-yl)-but-2-ene-1,4-diamine, hydrochloride salt (213.8 mg, 0.365 mmol) was neutralized with 1M NaOH (25 mL) and the free base was extracted with CHCl.sub.3. . .

DETD [1372] COMPOUND 160: 3-Aminomethyl-N.sup.1-(1H-benzoimidazol-2-ylmethyl)-N.sup.1-(S)-(5,6,7,8-tetrahydro-quinolin-8-yl)-but-2-ene-1,4-diamine Hydrochloride Salt

DETD [1444] Preparation of Carbonic Acid pyrrolidin-3-ylmethyl Ester Vinyl

Ester Hydrochloride: ##STR213##

DETD . . . was added THF (4 mL), Et.sub.3N (0.58 mL, 4.2 mmol), and a solution of carbonic acid pyrrolidin-3-ylmethyl ester vinyl ester hydrochloride (284 mg, 1.37 mmol) in THF (3 mL), and the mixture was stirred at room temperature for 21 h. The. . .

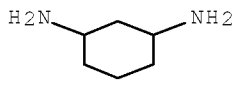
IT 65-85-0, Benzoic acid, reactions 75-31-0, Isopropylamine, reactions 79-33-4, L-Lactic acid, reactions 93-10-7, Quinoline-2-carboxylic acid 93-53-8, 2-Phenylpropionaldehyde 93-97-0, Benzoic anhydride 95-54-5, 1,2-Phenylenediamine, reactions 96-32-2, Methyl bromoacetate 98-97-5, 2-Pyrazinecarboxylic acid 98-98-6, Picolinic acid 100-46-9, Benzylamine, reactions 100-52-7, Benzaldehyde, reactions 100-58-3, Phenylmagnesium bromide 104-98-3, Urocanic acid 105-36-2, Ethyl bromoacetate 106-95-6, Allyl bromide, reactions 107-11-9, Allylamine 107-18-6, Allyl alcohol, reactions 110-63-4, 1,4-Butanediol, reactions 110-91-8, Morpholine, reactions 123-72-8, Butyraldehyde 124-02-7, Diallylamine 156-87-6, 3-Amino-1-propanol 273-21-2, 4-Azabenzimidazole 288-32-4, Imidazole, reactions 487-89-8, Indole-3-carboxaldehyde 504-02-9, 1,3-Cyclohexanedione 555-03-3, 3-Nitroanisole 592-57-4, 1,3-Cyclohexadiene 603-35-0, Triphenylphosphine, reactions 609-65-4, 2-Chlorobenzoyl chloride 616-29-5, 1,3-Diamino-2-hydroxypropane 616-30-8, 3-Amino-1,2-propanediol 617-52-7, Dimethyl itaconate 623-27-8, 1,4-Benzenedicarboxaldehyde 627-27-0, 3-Buten-1-ol 765-30-0, Cyclopropylamine 822-36-6, 4-Methylimidazole 826-34-6, Dimethyl cis-1,2-cyclopropanedicarboxylate 867-13-0, Triethyl phosphonoacetate 1074-82-4, Potassium phthalimide 1099-45-2, (Carbethoxymethylene)triphenylphosphorane 1121-60-4, Pyridine-2-carboxaldehyde 1126-09-6, Ethyl isonipecotate 1477-50-5, Indole-2-carboxylic acid 1694-92-4, 2-Nitrobenzenesulfonyl chloride 2605-67-6, Methyl (triphenylphosphoranylidene)acetate 2615-25-0, trans-1,4-Cyclohexanediamine 2859-68-9, 3-(2-Pyridyl)-1-propanol 3012-80-4, 1-Methyl-1H-benzimidazole-2-carboxaldehyde 3385-21-5, 1,3-Cyclohexanediamine 3433-37-2, 2-Piperidinemethanol 3752-24-7, 4,5,6,7-Tetrahydro-1H-benzimidazole 3920-50-1, Pyrazole-3-carboxaldehyde 3999-55-1, Diethyl trans-1,2-cyclopropanedicarboxylate 4023-02-3, 1H-Pyrazole-1-carboxamidine hydrochloride 4048-33-3, 6-Amino-1-hexanol 4606-65-9, 3-Piperidinemethanol 4760-34-3, N-Methyl-o-phenylenediamine 4856-97-7, 2-Hydroxymethylbenzimidazole 5006-66-6, 6-Hydroxynicotinic acid 5130-24-5, Vinyl chloroformate 5332-06-9, 4-Bromobutyronitrile 5332-24-1, 3-Bromoquinoline 5382-16-1, 4-Hydroxypiperidine 5414-21-1, 5-Bromovaleronitrile 5456-63-3, trans-2-Aminocyclohexanol hydrochloride 5731-17-9, (1-Benzylpyrrolidin-3-yl)methanol 5993-91-9, 2-(Aminomethyl)benzimidazole dihydrochloride 6602-32-0, 2-Bromo-3-pyridinol 6624-49-3, 3-Isoquinolinecarboxylic acid 6859-99-0, 3-Hydroxypiperidine 6976-17-6, 4-(Methylamino)butyric acid hydrochloride 7051-34-5, (Bromomethyl)cyclopropane 7153-66-4, (Z)-4-Chloro-2-butenylamine hydrochloride 7197-96-8, 2,3-Cycloheptenopyridine 10111-08-7, Imidazole-2-carboxaldehyde 13325-10-5, 4-Amino-1-butanol 13750-81-7, 1-Methyl-2-imidazolecarboxaldehyde 13958-93-5, 3,5-Dichloroisonicotinic acid 14080-23-0, 2-Cyanopyrimidine 14631-46-0, 8-Hydroxy-5,6,7,8-tetrahydroquinoline 16139-18-7, Aminoguanidine hydrochloride 20826-04-4, 5-Bromonicotinic acid 21905-86-2, Cinnoline-4-carboxylic acid 22059-21-8, 1-Aminocyclopropanecarboxylic acid 26690-80-2, (2-Hydroxyethyl)carbamic acid tert-butyl ester 29602-39-9, 2-[(2-Aminoethyl)amino]-5-nitropyridine 31106-82-8, 2-(Bromomethyl)pyridine hydrobromide 32673-41-9, 4-(Hydroxymethyl)imidazole hydrochloride 33036-62-3, 4-Bromobutan-1-ol 34413-35-9, 5,6,7,8-Tetrahydroquinoxaline 38666-30-7,

5,6,7,8-Tetrahydroimidazo[1,5-a]pyridine 42383-61-9, 2-Aminoimidazole sulfate 46153-01-9, 2-Methyl-5,6-dihydro-4H-imidazo[4,5,1-ij]quinoline 50910-54-8, trans-4-Aminocyclohexanol hydrochloride 53054-03-8, (2S)-5-Amino-2-(tert-butoxycarbonylamino)pentanoic acid tert-butyl ester 58885-58-8, (3-Hydroxypropyl)carbamic acid tert-butyl ester 61388-89-4, 2-Methyl-8-acetamidoquinoline 66715-65-9, 2-Pyridinesulfonyl chloride 68076-36-8, (4-Aminobutyl)carbamic acid tert-butyl ester 69610-41-9, N-(tert-Butoxycarbonyl)-L-prolinal 72998-92-6, 2-Chloromethyl-5,6-dimethyl-1H-benzimidazole 76513-69-4, [2-(Trimethylsilyl)ethoxy]methyl chloride 77369-59-6, 1-Amino-4-chloro-2-butyne hydrochloride 80567-69-7, 2-Chloromethyl-4-methyl-1H-benzimidazole 102089-74-7, (R)-N-(tert-Butoxycarbonyl)-2-phenylglycinol 104249-15-2, N-((E)-4-Bromo-2-butenyl)phthalimide 107430-29-5, 2-Chloromethyl-6-trifluoromethyl-1H-benzimidazole 117049-14-6, (S)-N-(tert-Butoxycarbonyl)-2-phenylglycinol 125163-05-5, 8-Hydroxy-4-methoxy-5,6,7,8-tetrahydroquinoline 130861-73-3, 2-Chloro-8-hydroxy-5,6,7,8-tetrahydroquinoline 156144-42-2, 2-Chloromethyl-5-fluoro-1H-benzimidazole 157634-00-9, 2-Hydroxymethylpiperidine-1-carboxylic acid tert-butyl ester 163798-87-6, 1-(tert-Butoxycarbonyl)-2-chloromethylbenzimidazole 229328-97-6, 3,5-Dichloroisonicotinoyl chloride 298181-83-6, 8-Amino-5,6,7,8-tetrahydroquinoline 369655-84-5, ((R)-5,6,7,8-Tetrahydroquinolin-8-yl)amine 369656-57-5, (S)-5,6,7,8-Tetrahydroquinolin-8-ylamine 405173-68-4, 2-Chloromethyl-4,5-dimethyl-1H-benzimidazole 405173-94-6, 2-Chloromethyl-7-fluoro-1H-benzimidazole 405174-39-2, 4-(4-Fluorophenyl)-1-[(2-trimethylsilanylethoxy)methyl]-1H-imidazole-2-carboxaldehyde 507228-47-9, [tert-Butoxycarbonylimino(4-oxopiperidin-1-yl)methyl]carbamic acid tert-butyl ester 558441-93-3, 4-[(1H-Benzimidazole-2-ylmethyl)(5,6,7,8-tetrahydroquinolin-8-yl)amino]butyraldehyde 558442-56-1, [[1-(tert-Butoxycarbonyl)benzimidazol-2-yl]methyl](5,6,7,8-tetrahydroquinolin-8-yl)[(4S)-4-phenyl-4-(tert-butoxycarbonylamino)butyl]amine 558442-84-5, N1-(1H-Benzimidazol-2-ylmethyl)-N1-(5,6,7,8-tetrahydroquinolin-8-yl)-N4-benzylcyclohexane-trans-1,4-diamine 558443-56-4, [[1-(tert-Butoxycarbonyl)-1H-benzimidazol-2-yl]methyl](5,6,7,8-tetrahydroquinolin-8-yl)(3-cyanopropyl)amine 558443-80-4, 2-[4-(tert-Butyldimethylsilanyloxy)-2-hydroxybutyl]isoindole-1,3-dione 558444-72-7, 2-[4-[((S)-5,6,7,8-Tetrahydroquinolin-8-yl)amino]butyl]isoindole-1,3-dione 558445-48-0, 2-Chloromethyl-4-methoxybenzimidazole-1-carboxylic acid tert-butyl ester 558446-25-6, N-(5,6,7,8-Tetrahydroquinolin-8-yl)butane-1,4-diamine 558447-10-2, N'-((S)-5,6,7,8-Tetrahydroquinolin-8-yl)butane-1,4-diamine 558447-26-0, N'-(1H-Benzimidazol-2-ylmethyl)-N'-((S)-5,6,7,8-tetrahydroquinolin-8-yl)butane-1,4-diamine 558447-80-6, 4-[[(1-Allyl-1H-benzimidazol-2-yl)methyl]((S)-5,6,7,8-tetrahydroquinolin-8-yl)amino]butylamine hydrochloride 558447-89-5, (1H-Benzimidazol-2-ylmethyl)((S)-5,6,7,8-tetrahydroquinolin-8-yl)amine 558447-98-6, 3-Aminomethyl-N-(1H-benzimidazol-2-ylmethyl)-N-(5,6,7,8-tetrahydroquinolin-8-yl)but-2-ene-1,4-diamine hydrochloride
(preparation of chemokine receptor binding benzimidazolylmethyl tetrahydroquinolinyl amines and related heterocyclic compds. with enhanced efficacy against AIDS and other disorders)

IT 3385-21-5, 1,3-Cyclohexanediamine
(preparation of chemokine receptor binding benzimidazolylmethyl tetrahydroquinolinyl amines and related heterocyclic compds. with enhanced efficacy against AIDS and other disorders)

RN 3385-21-5 USPATFULL

CN 1,3-Cyclohexanediamine (CA INDEX NAME)



L79 ANSWER 28 OF 38 USPATFULL on STN
ACCESSION NUMBER: 2003:146829 USPATFULL Full-text
TITLE: Methods and compounds for inhibiting mrp1
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	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 2003100576	A1	20030529		<--
	US 6743794	B2	20040601		
APPLICATION INFO.:	US 2002-130800	A1	20020521	(10)	<--
	WO 2000-US32443		20001211		

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ELI LILLY AND COMPANY, PATENT DIVISION, P.O. BOX 6288, INDIANAPOLIS, IN, 46206-6288
NUMBER OF CLAIMS: 71
EXEMPLARY CLAIM: 1
LINE COUNT: 14296
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention further relates to a method of inhibiting MRP1 in a mammal which comprises administering to a mammal in need thereof an effective amount of a compound of formula (I).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AI 20001211
DETD [0220] cxxxv. The compound is the hydrochloride salt.
DETD [0229] h) N-[3-(9-Chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-2-methylamino-acetamide hydrochloride
DETD [0232] k) 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-2-methyl-propionamide hydrochloride

DETD [0234] m) 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-acetamide hydrochloride

DETD [0238] q) N-[3-(9-Chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-2-phenyl-2-piperazin-1-yl-acetamide dihydrochloride

DETD [0240] s) N-[3-(9-Chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-2-methylamino-2-phenyl-acetamide hydrochloride

DETD [0253] ff) 1-Amino-cyclohexanecarboxylic acid [3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-amide hydrochloride

DETD [0260] mm) 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-2-cyclohexyl-acetamide hydrochloride

DETD [0261] nn) 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-2-cyclohexyl-acetamide hydrochloride

DETD [0282] iii) N-[3-(9-Chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclopentyl]-2-methylarnino-acetamide hydrochloride

DETD [0285] lll) 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclopentyl]-2-methyl-propionamide hydrochloride

DETD [0287] nnn) 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclopentyl]-acetamide hydrochloride

DETD [0291] rrr) N-[3-(9-Chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclopentyl]-2-phenyl-2-piperazin-1-yl-acetamide dihydrochloride

DETD [0293] ttt) N-[3-(9-Chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclopentyl]-2-methylamino-2-phenyl-acetamide hydrochloride

DETD [0306] gggg) 1-Amino-cyclohexanecarboxylic acid [3-(9-chloro-3-methyl4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclopentyl]-amide hydrochloride

DETD [0313] nnnn) 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclopentyl]-2-cyclohexyl-acetamide hydrochloride

DETD [0314] oooo) 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-2-cyclopentyl-acetamide hydrochloride

DETD [0374] For compounds in which het is pyrazole, the addition of 1-(3-dimethyl-aminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) to the reaction is preferred. The compound of formula XI is preferably the corresponding carboxylic acid and is employed. . .

DETD . . . of formula XIII by dissolving or suspending a compound of formula XVI in a suitable acidic solvent and adding hydroxylamine hydrochloride. Glacial acetic acid is a convenient acidic solvent and is typically preferred. The ester group is then hydrolyzed to the. . .

DETD [0389] Generically, the compound of formula XVIII and hydroxylamine hydrochloride are suspended or dissolved in a suitable solvent and a suitable base is added. After the reaction is complete, the. . .

DETD [0472] To a suspension of 5.00 g (26.5 mmol) of 3-nitrobenzylamine hydrochloride in 100 mL CH.sub.2Cl.sub.2 at room temperature was added 5.79 g (26.5 mmol) of di-t-butyl dicarbonate. To this was added. . .

DETD 5-((3S,1R)-3-Aminocyclohexyl)-9-chloro-3-methyl-H-isoxazolo[4,3-c]quinolin-4-one hydrochloride

DETD 5-((1S,3R)-3-aminocyclohexyl)-9-chloro-3-methyl-5H-isoxazolo[4,3-c]quinolin-4-one hydrochloride

DETD . . . the resulting solid dried overnight in vacuo which resulted in the isolation of 6.84 g (94%) of the desired ester hydrochloride. MS(S): (M+1).sup.+172.2 m/z.

DETD . . . a gas. After stirring the resulting solution for 30 min, triethyl amine (746 μL; 5.36 mmol; 2 equiv) and N,O-dimethylhydroxylamine hydrochloride (570 mg; 5.90 mmol; 2.2. equiv) were added and the solution stirred for 15 h. Water was added to the. . .

DETD 4-Amino-1-ethylcyclohexanecarboxylate hydrochloride

DETD trans-5-[3-(Aminomethyl)cyclohexyl]-9-chloro-3-methyl-5H-isoxazolo[4,3-c]quinolin-4-one hydrochloride

DETD . . . preparation 147 (16.9 g, 67.6 mmol) in H.sub.2O (35 mL), EtOH (35 mL), and ice (25 g) was added hydroxylamine hydrochloride (4.8 g, 74.4 mmol). Then, 169 mmol of 50% NaOH (6.76 g in 6.76 mL H.sub.2O) was

added with stirring.. . .
DETD N-t-Butyl-N'-(2-chloro-6-fluorobenzylidene)hydrazine hydrochloride
DETD [0594] A mixture of t-butyl hydrazine hydrochloride (1.24 g, 10 mmol) and 2-chloro-6-fluorobenzaldehyde (1.1 mL, 10 mmol) dissolved in acetic acid (5 mL) was stirred at 50°. . .
DETD Cis-3-(amino)-1-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexane hydrochloride
DETD 3-(2-Amino-trans-cyclohexyl)propionic acid methyl ester hydrochloride
DETD 3-(2-Amino-cis-cyclohexyl)propionic acid methyl ester hydrochloride
DETD Methyl 3-(2-aminocyclohexyl)propanoate hydrochloride
DETD 4-Methoxypicolinic acid hydrochloride
DETD . . . in 120 mL of tetrahydrofuran was added 12 mL (88.0 mmol) of triethylamine and 5.4 g (66.0 mmol) of dimethylamine hydrochloride. The reaction mixture was heated at 60° C. in a sealed tube for three hours, cooled to ambient temperature and. . .
DETD [0770] Benzoyl chloride (1.40 mL, 12.1 mmol) was added in a dropwise manner to a mixture of L-proline methyl ester hydrochloride (2.00 g, 12.1 mmol) and Et.sub.3N (4.20 mL, 30.2 mmol) in CH.sub.2Cl.sub.2 (40 mL) and the resulting mixture stirred overnight. . .
DETD [0773] Phenacetyl chloride (1.60 mL, 12.1 mmol) was added to a mixture of L-proline methyl ester hydrochloride (2.00 g, 12.1 mmol) and Et.sub.3N (4.20 mL, 30.2 mmol) in CH.sub.2Cl.sub.2 (40 mL) and the resulting mixture stirred overnight. . .
DETD . . . acid ethyl ester (2.54 g; 10.2 mmol) was reacted in a sealed tube, at rt., in CH.sub.2Cl.sub.2, overnight with N,N-dimethylamine hydrochloride (3.34 g; 41.0 mmol; 4 equiv) and Et.sub.3N (5.8 mL; 41.0 mmol; 4 equiv). The reaction solution was evaporated to. . .
DETD [0817] To a suspension of 5.00 g (26.5 mmol) of 3-nitrobenzylamine hydrochloride in 100 mL CH.sub.2Cl.sub.2 at rt. was added 5.79 g (26.5 mmol) of di-t-butyl dicarbonate. To this was added 8.13. . .
DETD 2-Amino-N-[3-(9-chloro-3-methyl4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-acetamide hydrochloride
DETD . . . solution of a compound from preparation 377 (0.05 g, 0.13 mmol) in acetic acid (5 mL) was treated with hydroxylamine hydrochloride (13 mg, 0.19 mmol). The solution was heated to reflux and stirred 5 hr. The reaction was then diluted in. . .
DETD . . . carboxamide

415 Ex 615	N-[(1R,3S)-3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]-quinolin-5-yl)cyclohexylmethyl]-2-(1-methyl-1H-imidazol-4-yl)acetamide MS (ion spray) 468 (M.sup.+), 466 (M.sup.- - 1)	1-methyl-4-irnidazole acetic acid hydrochloride	
416 Ex 615	3-Benzoyl-N-[(1R,3S)-3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexylmethyl]-benzamide MS (ion spray) 554 (M+), 552 (M.sup.- - 1)	3-benzoyl-benzoic acid	

417. . .
DETD . . . the combined extracts were dried over sodium sulfate. Concentration in vacuo left the crude acid which was combined with 1-(3-dimethyl-aminopropyl-3-ethylcarbodiimide hydrochloride (0.186 g, 0.00097 mol), 1-hydroxy-7-azabenzotriazole (0.133 g, 0.00098 mol) and 3,4,5-trimethoxybenzylamine (0.193 g, 0.00098 mol) in DMF (15 mL) and. . .
DETD . . . To a solution of the compound from Example 490 in denatured

ethanol (6 mL) was added a solution of methoxyamine hydrochloride (74.5 mg; 0.892 mmol; 4 equiv) and sodium acetate (73.1 mg; 0.892 mmol; 4 equiv) in water (1 mL). The. . .

DETD (1S,3R)-1-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-3-[((2S)-2-amino-2-phenylacetyl)amino]cyclohexane hydrochloride

DETD (1R,3S)-1-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-3-[((2S)-2-amino-2-phenylacetyl)amino]cyclohexane hydrochloride

DETD (1S,3R)-1-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-3-[((2R)-2-amino-2-phenylacetyl) amino]cyclohexane hydrochloride

DETD . . . mL of N,N-dimethylformamide. To this solution was added 23 mg (0.17 mmol) of 1-hydroxy-7-azabenzotriazole, 33 mg (0.17 mmol) of 1-(3-dimethyl-aminopropyl)-3-ethylcarbodiimide hydrochloride, 5 mg of 4-dimethylaminopyridine and 60 μL (0.42 mmol) of triethylamine. Yield=33 mg (53%) of the desired isomer as a. . .

DETD 1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid [3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexyl]amide hydrochloride

DETD 1,2,3,4-Tetrahydro-isoquinoline-3-carboxylic acid [3-(9chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-amide hydrochloride

DETD 2-Amino-N-{[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexylcarbamoyl]-phenylmethyl}-2-methylpropionamide hydrochloride

DETD [0965] A compound from Example 321 was deprotected in a manner similar to Example 638 and kept as the hydrochloride salt. MS(ES) calc'd: [M+H].sup.+=550.2 m/z; [M-H.sup.-=548.2 m/z; [M+Cl].sup.-=584.2 m/z. Found: 550.0 m/z; 548.0 m/z; 584.0 m/z.

DETD [0972] A solution of N-{[3-(3-acetyl-4-amino-5-chloro-2-oxohydroquinolyl)-cyclohexyl]-methyl}(phenylmethoxy)carboxamide (0.02 g, 0.04 mmol) in acetic acid (2 mL) was treated with hydroxylamine hydrochloride (3 mg, 0.046 mmol). The solution was heated to reflux and stirred 4 hr. The reaction was then diluted in. . .

DETD [0974] A solution of N-{[3-(3-acetyl-4-amino-5-chloro-2-oxohydroquinolyl)cyclohexyl]-methyl}(6-fluoro(3-pyridyl))carboxamide (0.035 g, 0.07 mmol) in acetic acid (5 mL) was treated with hydroxylamine hydrochloride (7.8 mg, 0.11 mmol). The solution was heated to reflux and stirred 3 hr. The reaction was then diluted in. . .

DETD N-[3-(9-Chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-2-methylamino-acetamide hydrochloride

DETD 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexyl]-2-methyl-propionamide hydrochloride

DETD 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexyl]-acetamide hydrochloride

DETD N-[3-(9-Chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexyl]-2-phenyl-2-piperazin-1-ylacetamide dihydrochloride

DETD N-[3-(9-Chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexyl]-2-methylamino-2-phenylacetamide hydrochloride

DETD 1-Aminocyclohexanecarboxylic acid [3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexyl]amide hydrochloride

DETD 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexyl]-2-cyclohexylacetamide hydrochloride

DETD 2-Amino-N-[3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexyl]-2-cyclohexylacetamide hydrochloride

DETD 2-Aminoindan-2-carboxylic acid [3-(9-chloro-3-methyl-4-oxo-5H-isoxazolo[4,3-c]quinolin-5-yl)cyclohexyl]amide hydrochloride

DETD 1-Amino-cyclopentanecarboxylic acid [3-(9-chloro-3-methyl-4-oxo-4H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-amide hydrochloride

DETD 1-Amino-cyclopropanecarboxylic acid [3-(9-chloro-3-methyl-4-oxo4H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexyl]-amide hydrochloride

DETD R(-)Amino-acetic acid [3-(9-chloro-3-methyl-4oxo4H-isoxazolo[4,3-c]quinolin-5-yl)-cyclohexylcarbamoyl]-phenyl-methyl ester hydrochloride

DETD S(+)Amino-acetic acid [3-(9-chloro-3-methyl-4-oxo-4H-isoxazolo[4,3-

c]quinolin-5-yl)-cyclohexylcarbamoyl]-phenyl-methyl ester hydrochloride

DETD . . . mg, 0.25 mmol), 1-hydroxy-7-azabenzo-triazole (34 mg, 0.25 mmol), N,N-diisopropylethyl amine (0.10 mL, 0.58 mmol), DMAP (5 mg, cat.), and N-benzylglycine hydrochloride (50 mg, 0.25 mmol) in DMF(6 mL) and the mixture stirred overnight at rt. The mixture was then concentrated in. . . EtOAc and treated with excess diethyl ether/hydrochloric acid. Concentration of this mixture to dryness allowed for quantitative recovery of the hydrochloride salt as an off white solid. MS(ES): (M+1).sup.+ 479.1, 481.2.

DETD . . . 638 (50 mg; 0.108 mmol) was dissolved in anhydrous dimethylformamide (10 mL) under a nitrogen atmosphere, mixed with 1-methyl-piperidine-4-carboxylic acid hydrochloride (58.0 mg; 0.323 mmol; 3 equiv), 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (61.8 mg; 0.323 mmol; 3 equiv), 2,4,6-trimethylpyridine (86 μL; 0.645 mmol; 6 equiv), and 1-hydroxy-7-azabenzotriazole (43.9 mg; 0.323 mmol; 3. . .

DETD . . . 5-(3-aminocyclohexyl)-9-chloro-3-methyl-5H-isoxazolo[4,3-c]quinolin4-one (50 mg; 0.151 mmol), N-phenylglycine (29.6 mg; 0.196 mmol; 1.3 equiv), 1-hydroxy-7-azabenzotriazole (26.7 mg; 0.196 mmol; 1.3 equiv), 1-[3-(dimethylamino)propyl[-3-ethylcarbodiimide hydrochloride (37.6 mg; 0.196 mmol; 1.3 equiv), and 2,4,6-trimethylpyridine (199 μL; 1.51 mmol; 10 equiv). After overnight stirring at room temperature,. . .

DETD . . . of material from Preparation 210 (100 mg; 0.301 mmol) in anhydrous DMF. Diisopropylethylamine (262 μL; 0.392 mmol; 5 equiv), 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (75.1 mg; 0.392 mmol; 1.3 equiv), and 1-hydroxy-7-azabenzotriazole (53.3 mg; 0.392 mmol; 1.3 equiv) were then added and the solution. . .

DETD . . . methyl amide (700 mg, 2.0 mmol) in 35 mL of dichloromethane was added 440 mg (2.4 mmol) of nicotinoyl chloride hydrochloride, 0.85 mL (6.0 mmol) of triethylamine and 5 mg of 4-dimethylaminopyridine. The reaction mixture was stirred overnight at ambient temperature,. . .

DETD . . . triethylamine, 43 mg (0.27 mmol) of 6-chloronicotinic acid, 36 mg (0.27 mmol) of 1-hydroxy-7-azabenzo-triazole, 51 mg (0.27 mmol) of 1-(3-dimethylamino-propyl)-3-ethyl-carbodiimide hydrochloride and 5 mg of 4-dimethylaminopyridine. The reaction mixture was stirred overnight at ambient temperature and concentrated to dryness. The residue. . .

IT 52-52-8, 1-Amino-1-cyclopentanecarboxylic acid 55-22-1, Pyridine-4-carboxylic acid, reactions 59-67-6, Pyridine-3-carboxylic acid, reactions 62-53-3, Aniline, reactions 69-72-7, Salicylic acid, reactions 75-64-9, tert-Butylamine, reactions 76-93-7, reactions 79-14-1, Glycolic acid, reactions 79-30-1, Isobutyryl chloride 87-62-7, 2,6-Dimethylphenylamine 90-04-0, 2-Methoxyphenylamine 90-52-8, 6-Methoxyquinolin-8-ylamine 92-54-6, 1-Phenylpiperazine 93-97-0, Benzoic anhydride 95-53-4, 2-Methylphenylamine, reactions 95-55-6, 2-Aminophenol 96-50-4, 2-Aminothiazole 98-09-9, Benzenesulfonyl chloride 98-88-4, Benzoyl chloride 98-97-5, 2-Pyrazinecarboxylic acid 98-98-6, Pyridine-2-carboxylic acid 99-03-6 99-59-2, 2-Methoxy-5-nitroaniline 100-07-2, 4-Methoxybenzoyl chloride 100-46-9, Benzylamine, reactions 100-51-6, Benzyl alcohol, reactions 100-53-8, Benzyl mercaptan 100-60-7, N-Methyl-N-cyclohexylamine 100-61-8, N-Methylaniline, reactions 103-49-1, Dibenzylamine 103-67-3, N-Methyl-N-benzylamine 103-71-9, Phenyl isocyanate, reactions 103-72-0, Phenyl thioisocyanate 103-76-4, 1-(2-Hydroxyethyl)piperazine 103-80-0, Phenacetyl chloride 103-82-2, Phenylacetic acid, reactions 104-01-8 104-94-9, 4-Methoxyphenylamine 106-49-0, 4-Methylphenylamine, reactions 108-40-7, 3-Methylthiophenol 108-44-1, 3-Methylphenylamine, reactions 108-91-8, Cyclohexylamine, reactions 108-98-5, Thiophenol, reactions 109-00-2, 3-Hydroxypyridine 109-01-3,

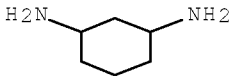
1-Methylpiperazine 110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions 121-90-4, 3-Nitrobenzoyl chloride 121-91-5, Isophthalic acid, reactions 122-01-0, 4-Chlorobenzoyl chloride 122-04-3, 4-Nitrobenzoyl chloride 123-75-1, Pyrrolidine, reactions 123-90-0, Thiomorpholine 124-68-5, 2-Amino-2-methyl-1-propanol 134-32-7, 1-Naphthylamine 142-08-5, 2-Hydroxypyridine 329-15-7, 4-Trifluoromethylbenzoyl chloride 331-25-9 348-52-7, 1-Fluoro-2-iodobenzene 348-54-9, 2-Fluoroaniline 360-03-2 371-40-4, 4-Fluoroaniline 371-42-6, 4-Fluorothiophenol 372-19-0, 3-Fluoroaniline 372-39-4, 3,5-Difluoroaniline 387-45-1, 2-Chloro-6-fluorobenzaldehyde 393-52-2, 2-Fluorobenzoyl chloride 393-55-5, 2-Fluoronicotinic acid 395-35-7, p-Trifluoromethylmandelic acid 402-65-3, 2-Fluoroisonicotinic acid 402-66-4, 5-Fluoronicotinic acid 403-43-0, 4-Fluorobenzoyl chloride 403-45-2, 6-Fluoronicotinic acid 405-50-5 407-22-7, 2-Fluoro-6-methylpyridine 434-75-3, 2-Chloro-6-fluorobenzoic acid 446-52-6, o-Fluorobenzaldehyde 462-08-8, 3-Aminopyridine 467-69-6, 9-Hydroxy-9-fluorenecarboxylic acid 486-74-8, Quinoline-4-carboxylic acid 498-95-3, Nipecotic acid 500-22-1, 3-Pyridinecarboxaldehyde 501-53-1 501-81-5, 2-(3-Pyridyl)acetic acid 501-97-3, 3-(4-Hydroxyphenyl)propionic acid 504-24-5, 4-Aminopyridine 504-29-0, 2-Aminopyridine 527-69-5, 2-Furoyl chloride 536-90-3, 3-Methoxyaniline 552-63-6, DL-Tropic acid 573-03-5, 4-Fluoro-1-naphthoic acid 579-18-0, 3-Benzoylbenzoic acid 583-08-4, Nicotinuric acid 586-75-4, 4-Bromobenzoyl chloride 591-27-5, 3-Aminophenol 594-61-6, 2-Methyllactic acid 603-80-5, 2-Methyl-3-hydroxybenzoic acid 609-65-4, 2-Chlorobenzoyl chloride 611-71-2, D-(-)-Mandelic acid 611-73-4, Benzoylformic acid 611-95-0, 4-Benzoylbenzoic acid 612-41-9, 2-Nitrocinnamic acid 612-62-4, 2-Chloroquinoline 615-18-9, 2-Chlorobenzoxazole 615-20-3, 2-Chlorobenzothiazole 618-46-2, 3-Chlorobenzoyl chloride 619-45-4, 4-Aminobenzoic acid methyl ester 620-23-5 626-58-4, 4-Methylpiperidine 626-64-2, 4-Hydroxypyridine 638-29-9, Valeryl chloride 645-45-4, Hydrocinnamoyl chloride 684-07-1 701-97-3, Cyclohexanepropionic acid 765-30-0, Cyclopropylamine 771-50-6, Indole-3-carboxylic acid 824-94-2, p-Methoxybenzyl chloride 826-55-1 830-96-6, 1H-Indole-3-propanoic acid 874-60-2, 4-Methylbenzoyl chloride 879-18-5, Naphthalene-1-carbonyl chloride 930-68-7, 2-Cyclohexen-1-one 933-88-0, 2-Methylbenzoyl chloride 934-60-1, 6-Methylpicolinic acid 951-82-6, 3,4,5-Trimethoxyphenylacetic acid 955-40-8, N-Benzyl-L-proline ethyl ester 1003-03-8, Cyclopentylamine 1118-68-9, N,N-Dimethylglycine 1120-88-3, 4-Methylpyridazine 1121-60-4, 2-Pyridinecarboxaldehyde 1122-96-9, 4-Methoxypyridine N-oxide 1129-28-8, Methyl 3-(bromomethyl)benzoate 1135-67-7 1148-11-4, N-Carbobenzyloxy-L-proline 1477-50-5, Indole-2-carboxylic acid 1578-63-8, .α.-Fluorophenylacetic acid 1710-98-1, 4-tert-Butylbenzoyl chloride 1711-02-0, 4-Iodobenzoyl chloride 1711-05-3, 3-Methoxybenzoyl chloride 1711-06-4, 3-Methylbenzoyl chloride 1711-07-5, 3-Fluorobenzoyl chloride 1711-09-7, 3-Bromobenzoyl chloride 1776-53-0, 4-Amino-1-cyclohexanecarboxylic acid 1798-09-0, 3-Methoxyphenylacetic acid 1821-12-1, 4-Phenylbutyric acid 1877-73-2, 3-Nitrophenylacetic acid 1885-14-9, Phenyl chloroformate 1912-48-7, 1-Methyl-3-indoleacetic acid 1918-77-0, 2-Thiopheneacetic acid 1939-99-7, .α.-Toluenesulfonyl chloride 2051-95-8, 3-Benzoylpropionic acid 2124-55-2, Indole-4-carboxylic acid 2133-40-6, L-Proline methyl ester hydrochloride 2215-77-2, 4-Phenoxybenzoic acid 2243-83-6, Naphthalene-2-carbonyl chloride 2251-65-2, 3-Trifluoromethylbenzoyl chloride 2392-54-3 2398-81-4, Nicotinic acid N-oxide 2516-34-9, Cyclobutylamine 2557-77-9, 3-Fluorothiophenol 2719-27-9, Cyclohexylcarbonyl chloride 2756-85-6, 1-Amino-1-cyclohexanecarboxylic acid 2768-42-5 2900-27-8 2935-35-5

2975-41-9, 2-Aminoindan 3128-05-0, 3-Oxocyclopentaneacetic acid 3173-56-6, Benzyl isocyanate 3222-47-7, 6-Methylnicotinic acid 3222-49-9, 5-Methylnicotinic acid 3222-56-8, 2-Methylnicotinic acid 3262-72-4 3282-30-2, Pivaloyl chloride 3385-21-5, 1,3-Diaminocyclohexane 3441-03-0, Methyl 3-(chlorocarbonyl)benzoate 3535-37-3, 3,4-Dimethoxybenzoyl chloride 3622-23-9, 2,6-Dichlorobenzothiazole 3684-12-6 3724-19-4, 3-(3-Pyridyl)propionic acid 3731-52-0, 3-(Aminomethyl)pyridine 3739-38-6, 3-Phenoxybenzoic acid 3863-11-4, 3,4-Difluoroaniline 3934-20-1, 2,4-Dichloropyrimidine 3966-30-1 3966-32-3 4100-13-4, 1,2,3-Thiadiazole-4-carboxylic acid 4110-80-9 4341-76-8, Ethyl 2-butynoate 4521-61-3, 3,4,5-Trimethoxybenzoyl chloride 4530-20-5, N-tert-Butoxycarbonylglycine 4595-59-9, 5-Bromopyrimidine 4595-60-2, 2-Bromopyrimidine 4684-94-0, 6-Chloro-2-pyridinecarboxylic acid 4755-50-4, 4-Dimethylaminobenzoyl chloride 4870-65-9, .α.-Bromophenylacetic acid 5006-22-4, Cyclobutylcarbonyl chloride 5166-67-6, Ethyl 1-methylnipecotate 5271-67-0, 2-Thiophenecarbonyl chloride 5326-23-8, 6-Chloronicotinic acid 5382-16-1, 4-Hydroxypiperidine 5398-44-7, 2,6-Dichloroisonicotinic acid 5426-55-1 5452-35-7, Cycloheptylamine 5470-22-4, 4-Chloropicolinic acid 5720-07-0, 4-Methoxyphenylboronic acid 5813-64-9, Neopentylamine 6064-63-7, 2-Hydroxycaproic acid 6068-72-0, 4-Cyanobenzoyl chloride 6120-95-2 6313-54-8, 2-Chloroisonicotinic acid 6342-19-4 6368-20-3 6404-31-5, N-Carbobenzyloxy-D-proline 6419-36-9, 3-Pyridylacetic acid hydrochloride 6480-68-8, 3-Quinolinecarboxylic acid 6602-54-6 6622-91-9, 4-Pyridylacetic acid hydrochloride 6921-34-2, Benzylmagnesium chloride 6973-60-0, N-Methylpyrrole-2-carboxylic acid 7021-09-2, 2-(2-Methoxyphenyl)acetic acid 7031-23-4, 3-Methylthiopropionyl chloride 7322-88-5, (S)-(+)-O-Acetylmandelic acid 7326-19-4, D-3-Phenyllactic acid 7377-26-6, Methyl 4-(chlorocarbonyl)benzoate 7400-27-3, tert-Butyl hydrazine hydrochloride 7418-65-7, 4-Aminonicotinic acid 7472-67-5 7782-24-3, (S)-(+)-2-Phenylpropionic acid 7782-26-5 7785-26-4 10002-29-6 10333-11-6 10351-19-6, (4-Pyridylthio)acetic acid 10400-19-8, Nicotinoyl chloride 10490-07-0 10502-44-0, p-Methoxymandelic acid 10541-83-0, 4-(Methylamino)benzoic acid
(preparation of N-isoxazoloquinolinylcyclohexylcarboxamides and analogs as MRP1 inhibitors)

IT 3385-21-5, 1,3-Diaminocyclohexane
(preparation of N-isoxazoloquinolinylcyclohexylcarboxamides and analogs as MRP1 inhibitors)

RN 3385-21-5 USPATFULL

CN 1,3-Cyclohexanediamine (CA INDEX NAME)



L79 ANSWER 29 OF 38 USPATFULL on STN

ACCESSION NUMBER: 2003:134820 USPATFULL Full-text

TITLE: Heterocycle substituted purine derivatives as potent antiproliferative agents

INVENTOR(S): Trova, Michael Peter, Schenectady, NY, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003092909	A1	20030515	<--
	US 6812232	B2	20041102	
APPLICATION INFO.:	US 2002-237530	A1	20020906 (10)	<--

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2001-318569P	20010911 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Michael L. Goldman, NIXON PEABODY LLP, Clinton Square, P.O. Box 31051, Rochester, NY, 14603-1051
NUMBER OF CLAIMS: 29
EXEMPLARY CLAIM: 1
LINE COUNT: 6821
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The compounds of the present invention are 2,6,9-trisubstituted purine derivatives which are inhibitors of cyclin/cdk complexes. The compounds of the current invention also are potent inhibitors of human cellular proliferation. As such, the compounds of the present invention constitute pharmaceutical compositions with a pharmaceutically acceptable carrier. Such compounds are useful in treating a disorder mediated by elevated levels of cell proliferation in a mammal compared to a healthy mammal by administering to such mammal an effective amount of the compound. Examples of the compounds of the present invention are represented by the following chemical structures: ##STR1##

with Y, V, A, R.sub.1, R.sub.2, R.sub.3, R.sub.4, R.sub.7, and n.sub.1 defined herein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

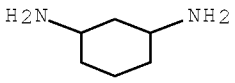
DETD [1544] To compound 4 (0.12 g, 0.27 mmol) was added 3-aminophenylboronic acid hydrochloride (0.12 g, 0.69 mmol), and Pd(PPh.sub.3).sub.4 (0.09 g, 0.75 mmol) in a sealed tube filled with argon. To this mixture. . .

DETD [1554] To compound 3 (0.26 g, 0.67 mmol) was added trans-4-aminocyclohexanol hydrochloride (0.62 g, 4.11 mmol), Et.sub.3N (0.58 mL, 4.16 mmol), and ethanol (5 mL). The mixture was heated for 5 h. . .

DETD [1575] Compound 72 (0.15 g, 0.40 mmol), trans-4-aminocyclohexanol hydrochloride (0.31 g, 1.99 mmol), Et.sub.3N (0.11 mL, 0.8 mmol), and EtOH (5 mL) were combined and heated in a sealed tube at 155° C. for 4 d. Additional trans-4-aminocyclohexanol hydrochloride (0.34 g, 2.2 mmol) and triethylamine (0.60 mL, 4.3 mmol) were added and the heat was resumed at 155° C.. . .

IT 75-30-9 92-69-3, [1,1'-Biphenyl]-4-ol 92-92-2, [1,1'-Biphenyl]-4-carboxylic acid 98-80-6 103-71-9, reactions 107-08-4, 1-Iodopropane 107-15-3, 1,2-Ethanediamine, reactions 108-30-5, Succinic anhydride, reactions 109-04-6 109-76-2, 1,3-Propanediamine 110-60-1, 1,4-Butanediamine 123-38-6, Propionaldehyde, reactions 123-72-8, Butyraldehyde 513-48-4, 2-Iodobutane 605-65-2 619-58-9 623-00-7 624-28-2, 2,5-Dibromopyridine 626-55-1 696-40-2 768-35-4 1066-45-1, Trimethyltin chloride 1120-87-2 1121-22-8, trans-1,2-Cyclohexanediamine 1423-26-3 1436-59-5, cis-1,2-Cyclohexanediamine 1461-22-9, Tributyltin chloride 1489-69-6, Cyclopropanecarboxaldehyde 1556-18-9, Iodocyclopentane 1679-18-1 1696-17-9 1765-93-1 2156-04-9 2615-25-0, trans-1,4-Cyclohexanediamine 3218-36-8, [1,1'-Biphenyl]-4-carboxaldehyde

3385-21-5, 1,3 Cyclohexanediamine 3815-20-1,
[1,1'-Biphenyl]-4-carboxamide 3900-89-8 3959-07-7, 4-Bromobenzylamine
4023-34-1, Cyclopropanoyl chloride 4530-20-5 5451-40-1,
2,6-Dichloropurine 5720-05-8 5720-07-0 5856-63-3 6165-68-0
6165-69-1 6271-78-9 7144-05-0, 4-Piperidinemethanamine 10316-79-7
10365-98-7 13331-23-2 13331-27-6 14047-29-1 15761-38-3
17933-03-8 23138-64-9 24358-62-1 25487-66-5 27489-62-9
39546-32-2, 4-Piperidinecarboxamide 39684-80-5 50910-54-8
55499-43-9 55552-70-0 59020-10-9 63503-60-6 73918-56-6
78887-39-5 79286-79-6, 3-Pyrrolidinamine 85006-23-1 89878-14-8
98437-24-2 107099-99-0 115298-62-9 124252-41-1 144432-85-9
146552-71-8 162607-15-0 162607-18-3 162607-20-7 172975-69-8
269410-09-5
(preparation of biarylmethylaminopurines as potent cyclin/CDK inhibitors and
antiproliferative agents)
IT 3385-21-5, 1,3 Cyclohexanediamine
(preparation of biarylmethylaminopurines as potent cyclin/CDK inhibitors and
antiproliferative agents)
RN 3385-21-5 USPATFULL
CN 1,3-Cyclohexanediamine (CA INDEX NAME)



L79 ANSWER 30 OF 38 USPATFULL on STN
ACCESSION NUMBER: 2003:127691 USPATFULL Full-text
TITLE: NITROGEN SUBSTITUTED BIARYL PURINE DERIVATIVES AS POTENT ANTIPROLIFERATIVE AGENTS
INVENTOR(S): Trova, Michael Peter, Schenectady, NY, UNITED STATES

	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 2003087906	A1	20030508		<--
	US 6667311	B2	20031223		
APPLICATION INFO.:	US 2001-950543	A1	20010911	(9)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Michael L. Goldman, NIXON PEABODY LLP, Clinton Square, P.O. Box 31051, Rochester, NY, 14603
NUMBER OF CLAIMS: 35
EXEMPLARY CLAIM: 1
LINE COUNT: 6666
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The compounds of the present invention are 2,6,9-trisubstituted purine derivatives which are inhibitors of cyclin/cdk complexes. The compounds of the current invention also are potent inhibitors of human cellular proliferation. As such, the compounds of the present invention constitute pharmaceutical compositions with a pharmaceutically acceptable carrier. Such compounds are useful in treating a disorder mediated by elevated levels of cell proliferation in a mammal compared to a healthy mammal by administering to such mammal an effective amount of the compound. Examples of the

compounds of the present invention are represented by the following chemical structures: ##STR1##

with X, Y, D, Q, V, A, R.sub.1, R.sub.2, R.sub.3, R.sub.4, and n.sub.1 defined herein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD [1401] To compound 4 (0.12 g, 0.27 mmol) was added 3-aminophenylboronic acid hydrochloride (0.12 g, 0.69 mmol), and Pd(PPh.sub.3).sub.4 (0.09 g, 0.75 mmol) in a sealed tube filled with argon. To this mixture. . .

DETD [1411] To compound 3 (0.26 g, 0.67 mmol) was added trans-4-aminocyclohexanol hydrochloride (0.62 g, 4.11 mmol), Et.sub.3N (0.58 mL, 4.16 mmol), and ethanol (5 mL). The mixture was heated for 5 h. . .

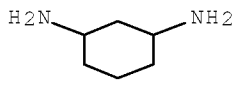
DETD [1432] Compound 72 (0.15 g, 0.40 mmol), trans-4-aminocyclohexanol hydrochloride (0.31 g, 1.99 mmol), Et.sub.3N (0.11 mL, 0.8 mmol), and EtOH (5 mL) were combined and heated in a sealed tube at 155° C. for 4 d. Additional trans-4-aminocyclohexanol hydrochloride (0.34 g, 2.2 mmol) and triethylamine (0.60 mL, 4.3 mmol) were added and the heat was resumed at 155° C.. . .

IT 75-30-9 92-69-3, [1,1'-Biphenyl]-4-ol 92-92-2, [1,1'-Biphenyl]-4-carboxylic acid 98-80-6 103-71-9, reactions 107-08-4, 1-Iodopropane 107-15-3, 1,2-Ethanediamine, reactions 108-30-5, Succinic anhydride, reactions 109-04-6 109-76-2, 1,3-Propanediamine 110-60-1, 1,4-Butanediamine 123-38-6, Propionaldehyde, reactions 123-72-8, Butyraldehyde 513-48-4, 2-Iodobutane 605-65-2 619-58-9 623-00-7 624-28-2, 2,5-Dibromopyridine 626-55-1 696-40-2 768-35-4 1066-45-1, Trimethyltin chloride 1120-87-2 1121-22-8 1423-26-3 1436-59-5 1461-22-9, Tributyltin chloride 1489-69-6, Cyclopropanecarboxaldehyde 1556-18-9, Iodocyclopentane 1679-18-1 1696-17-9 1765-93-1 2156-04-9 2615-25-0 3218-36-8, [1,1'-Biphenyl]-4-carboxaldehyde 3385-21-5, 1,3 Cyclohexanediamine 3815-20-1, [1,1'-Biphenyl]-4-carboxamide 3900-89-8 3959-07-7, 4-Bromobenzylamine 4023-34-1, Cyclopropanoyl chloride 4530-20-5 5451-40-1 5720-05-8 5720-07-0 5856-63-3 6165-68-0 6165-69-1 6271-78-9 7144-05-0, 4-Piperidinemethanamine 10316-79-7 10365-98-7 13331-23-2 13331-27-6 14047-29-1 15761-38-3 17933-03-8 23138-64-9 24358-62-1 25487-66-5 27489-62-9 39546-32-2, 4-Piperidinecarboxamide 39684-80-5 50910-54-8 55499-43-9 55552-70-0 59020-10-9 63503-60-6 73918-56-6 78887-39-5 79286-79-6, 3-Pyrrolidinamine 85006-23-1 89878-14-8 98437-24-2 107099-99-0 115298-62-9 124252-41-1 144432-85-9 146552-71-8 162607-15-0 162607-18-3 162607-20-7 172975-69-8 269410-09-5
(preparation of biarylmethylaminopurines as potent cyclin/CDK inhibitors and antiproliferative agents)

IT 3385-21-5, 1,3 Cyclohexanediamine
(preparation of biarylmethylaminopurines as potent cyclin/CDK inhibitors and antiproliferative agents)

RN 3385-21-5 USPATFULL

CN 1,3-Cyclohexanediamine (CA INDEX NAME)



L79 ANSWER 31 OF 38 USPATFULL on STN

ACCESSION NUMBER:	2002:172503 USPATFULL	Full-text		
TITLE:	Biaryl substituted purine derivatives as potent antiproliferative agents			
INVENTOR(S):	Trova, Michael Peter, Schenectady, NY, UNITED STATES			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002091263	A1	20020711	<--
	US 6969720	B2	20051129	
APPLICATION INFO.:	US 2001-950549	A1	20010911 (9)	<--
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2000-493790, filed on 28 Jan 2000, PENDING			
	NUMBER		DATE	
PRIORITY INFORMATION:	US 1999-124829P		19990317 (60)	<--
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	APPLICATION			
LEGAL REPRESENTATIVE:	Michael L. Goldman, NIXON PEABODY LLP, Clinton Square, P.O. Box 31051, Rochester, NY, 14603			
NUMBER OF CLAIMS:	36			
EXEMPLARY CLAIM:	1			
LINE COUNT:	6598			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The compounds of the present invention are 2,6,9-trisubstituted purine derivatives which are inhibitors of cyclin/cdk complexes. The compounds of the current invention also are potent inhibitors of human cellular proliferation. As such, the compounds of the present invention constitute pharmaceutical compositions with a pharmaceutically acceptable carrier. Such compounds are useful in treating a disorder mediated by elevated levels of cell proliferation in a mammal compared to a healthy mammal by administering to such mammal an effective amount of the compound. Examples of the compounds of the present invention are represented by the following chemical structures: ##STR1##

with X, Y, V, A, R.sub.1, R.sub.2, R.sub.3, R.sub.4, and n.sub.1 defined herein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD [1366] To compound 4 (0.12 g, 0.27 mmol) was added 3-aminophenylboronic acid hydrochloride (0.12 g, 0.69 mmol), and Pd(PPh.sub.3).sub.4 (0.09 g, 0.75 mmol) in a sealed tube filled with argon. To this mixture. . .

DETD [1376] To compound 3 (0.26 g, 0.67 mmol) was added trans-4-aminocyclohexanol hydrochloride (0.62 g, 4.11 mmol), Et.sub.3N (0.58 mL, 4.16 mmol), and ethanol (5 mL). The mixture was heated for 5 h. . .

DETD [1397] Compound 72 (0.15 g, 0.40 mmol), trans-4-aminocyclohexanol hydrochloride (0.31 g, 1.99 mmol), Et.sub.3N (0.11 mL, 0.8 mmol), and EtOH (5 mL) were combined and heated in a sealed tube at 155° C.

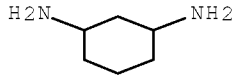
for 4 d. Additional trans-4-aminocyclohexanol hydrochloride (0.34 g, 2.2 mmol) and triethylamine (0.60 mL, 4.3 mmol) were added and the heat was resumed at 155° C.. . .

IT 75-30-9, 2-Iodopropane 79-03-8, Propionyl chloride 92-69-3, 4-Phenylphenol 92-92-2, 4-Phenylbenzoic acid 96-20-8, 2-Amino-1-butanol 98-80-6, Phenylboronic acid 103-71-9, Phenyl isocyanate, reactions 107-08-4, 1-Iodopropane 108-30-5, Succinic anhydride, reactions 109-04-6, 2-Bromopyridine 109-76-2, 1,3-Propanediamine 110-60-1, 1,4-Butanediamine 123-38-6, Propionaldehyde, reactions 123-72-8, Butyraldehyde 513-48-4, 2-Iodobutane 605-65-2 619-58-9, 4-Iodobenzoic acid 623-00-7, 4-Bromobenzonitrile 624-28-2, 2,5-Dibromopyridine 626-55-1, 3-Bromopyridine 696-40-2, 3-Iodobenzylamine 768-35-4, 3-Fluorobenzeneboronic acid 1121-22-8, trans-1,2-Diaminocyclohexane 1423-26-3, 3-(Trifluoromethyl)phenylboronic acid 1436-59-5, cis-1,2-Diaminocyclohexane 1489-69-6, Cyclopropanecarboxaldehyde 1556-18-9, Iodocyclopentane 1679-18-1, 4-Chlorobenzeneboronic acid 1696-17-9 1765-93-1, 4-Fluorobenzeneboronic acid 2156-04-9, 4-Vinylphenylboronic acid 2615-25-0, trans-1,4-Diaminocyclohexane 3218-36-8, 4-Biphenylcarboxaldehyde 3385-21-5, 1,3-Cyclohexanediamine 3815-20-1, [1,1'-Biphenyl]-4-carboxamide 3900-89-8, 2-Chlorobenzeneboronic acid 3959-07-7, 4-Bromobenzylamine 4023-34-1, Cyclopropanecarbonyl chloride 4530-20-5, BOC-glycine 5451-40-1, 2,6-Dichloropurine 5720-05-8, 4-Methylbenzeneboronic acid 5720-07-0, 4-Methoxyphenylboronic acid 5856-63-3, (R)-(-)-2-Amino-1-butanol 6165-68-0, 2-Thiopheneboronic acid 6165-69-1, 3-Thiopheneboronic acid 6271-78-9, 6-Chloronicotinamide 10316-79-7 10365-98-7, 3-Methoxyphenylboronic acid 13331-23-2, Furan-2-boronic acid 13331-27-6 14047-29-1, 4-Carboxyphenylboronic acid 15761-38-3, BOC-L-alanine 17933-03-8, 3-Tolylboronic acid 23138-64-9, 3-Acetylphenyl isocyanate 24358-62-1 25487-66-5, 3-Carboxyphenylboronic acid 32316-92-0, 2-Naphthaleneboronic acid 39546-32-2, 4-Piperidinecarboxamide 39684-80-5 50910-54-8, trans-4-Aminocyclohexanol hydrochloride 55499-43-9, 3,4-Dimethylbenzeneboronic acid 55552-70-0, Furan-3-boronic acid 59020-10-9, 3-(Tributylstannyl)pyridine 63503-60-6, 3-Chlorophenylboronic acid 73918-56-6 78887-39-5, 3-Acetamidophenylboronic acid 79286-79-6, 3-Aminopyrrolidine 85006-23-1, 3-Aminophenylboronic acid hydrochloride 89878-14-8, Diethyl(3-pyridyl)borane 98437-24-2 107099-99-0, 2,5-Dimethoxyphenylboronic acid 124252-41-1, 4-(Tributylstannyl)pyridine 144432-85-9, 3-Chloro-4-fluorobenzeneboronic acid 149632-73-5 162607-15-0, 4-Methylthiophene-2-boronic acid 162607-18-3, 5-Chloro-2-thiopheneboronic acid 162607-20-7, 5-Methyl-2-thiopheneboronic acid 172975-69-8, 3,5-Dimethylphenylboronic acid 269410-09-5
(preparation of 2,6,9-trisubstituted purine derivs. for therapeutic use as potent antiproliferative agents)

IT 3385-21-5, 1,3-Cyclohexanediamine
(preparation of 2,6,9-trisubstituted purine derivs. for therapeutic use as potent antiproliferative agents)

RN 3385-21-5 USPATFULL

CN 1,3-Cyclohexanediamine (CA INDEX NAME)



L79 ANSWER 32 OF 38 USPATFULL on STN
ACCESSION NUMBER: 2001:171145 USPATFULL Full-text
TITLE: Indeno [1,2-c]pyrazol-4-ones and their uses
INVENTOR(S): Nugiel, David A., Cherry Hill, NJ, United States
Carini, David J., Wilmington, DE, United States
DiMeo, Susan V., Wilmington, DE, United States
Yue, Eddy W., Landenberg, PA, United States

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2001027195	A1	20011004	<--
	US 6407103	B2	20020618	
APPLICATION INFO.:	US 2000-731304	A1	20001206 (9)	<--

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2000-639618, filed on 15 Aug 2000, PENDING Continuation of Ser. No. US 1999-295078, filed on 20 Apr 1999, ABANDONED

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1998-82476P	19980421 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Dupont Pharmaceuticals Company, Legal Department - Patents, 1007 Market Street, Wilmington, DE, 19898
NUMBER OF CLAIMS: 58
EXEMPLARY CLAIM: 1
LINE COUNT: 7875
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the synthesis of a new class of indeno[1,2-c]pyrazol-4-ones of formula (I): ##STR1##

that are potent inhibitors of the class of enzymes known as cyclin dependent kinases, which relate to the catalytic subunits cdk1-9 and their regulatory subunits know as cyclins A-H.

This invention also provides a novel method of treating cancer or other proliferative diseases by administering a therapeutically effective amount of one of these compounds or a pharmaceutically acceptable salt form thereof. Alternatively, one can treat cancer or other proliferative diseases by administering a therapeutically effective combination of one of the compounds of the present invention and one or more other known anti-cancer or anti-proliferative agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD [0739] Step 1. Synthesis of 29A from 4-acetylpiperidine hydrochloride.
DETD [0740] A solution of 4-acetylpiperidine hydrochloride (8.18 g, 0.05 mol) in THF (100 mL) at 0° C. was treated with triethylamine (13.93 mL, 0.1 mol) and. . .
DETD . . . of 3.82 g (6.6 mmol) of 35, 0.64 mL (13.2 mmol) of hydrazine monohydrate, 0.090 g (1.32 mmol) of hydrazine hydrochloride, and 130 mL of ethanol was refluxed for 18 h. While still at reflux the solution was diluted by the. . .
DETD . . . 4.43 g (7.7 mmol) of 35 (example CCX), 3.15 g (20.7 mnmol) of 4-methoxybenzylhydrazine, 0.29 g (1.50 mmol) of 4-methoxybenzylhydrazine

hydrochloride, and 150 mL of ethanol was refluxed for 22 h. While the reaction mixture was maintained at reflux 30 mL. . .

DETD [0908] A solution of 0.18 g (0.25 mmol) of 39, 0.27 g (2.5 mmol) of methyl acetimidate hydrochloride, 0.31 g (2.5 mmol) of 4-dimethylaminopyridine, and 10 mL of methanol was refluxed for 48 h. To the hot solution. . .

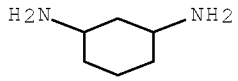
IT 57-14-7, 1,1-Dimethylhydrazine 62-53-3, Aniline, reactions 67-64-1, Acetone, reactions 74-89-5, Methylamine, reactions 75-04-7, Ethylamine, reactions 75-07-0, Acetaldehyde, reactions 79-03-8, Propionyl chloride 79-04-9, Chloroacetyl chloride 79-22-1, Methyl chloroformate 79-30-1, 2-Methylpropanoyl chloride 93-05-0, 4-(Diethylamino)aniline 96-54-8 98-86-2, Acetophenone, reactions 100-06-1 100-46-9, Benzylamine, reactions 103-76-4, 4-(2-Hydroxyethyl)piperazine 103-80-0, Phenylacetyl chloride 108-00-9, N,N-Dimethylethylenediamine 108-91-8, Cyclohexylamine, reactions 109-01-3 109-04-6, 2-Bromopyridine 109-73-9, Butylamine, reactions 109-89-7, Diethylamine, reactions 110-85-0, Piperazine, reactions 110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions 111-49-9, Homopiperidine 122-80-5, 4-(Acetamido)aniline 123-75-1, Pyrrolidine, reactions 123-90-0, Thiomorpholine 124-40-3, Dimethylamine, reactions 140-31-8, 4-(2-Aminoethyl)piperazine 140-69-2, 4-Methoxybenzylhydrazine 141-75-3, Butyryl chloride 326-91-0, 2-Thenoyltrifluoroacetone 350-03-8, 3-Acetylpyridine 383-63-1, Ethyl trifluoroacetate 505-66-8, Homopiperazine 527-72-0, 2-Thiophenecarboxylic acid 579-74-8 618-40-6, 1-Methyl-1-phenylhydrazine 619-84-1, 4-(Dimethylamino)benzoic acid 641-70-3, 3-Nitrophthalic Anhydride 693-11-8, 4-(Dimethylamino)butyric acid 937-30-4, 4'-Ethylacetophenone 1005-56-7, Phenyl thionochloroformate 1122-54-9, 4-Acetylpyridine 1131-62-0 1436-59-5, cis-1,2-Diaminocyclohexane 1676-63-7, 4'-Ethoxyacetophenone 1778-09-2, 4'-Methylthioacetophenone 1885-14-9, Phenyl chloroformate 2011-48-5, 4-Methoxybenzylhydrazine hydrochloride 2038-03-1, 4-(2-Aminoethyl)morpholine 2124-31-4, 4'-(N,N-Dimethylamino)acetophenone 2213-43-6, 1-Aminopiperidine 2706-56-1, 2-(2-Aminoethyl)pyridine 2932-65-2, 4'-Propylacetophenone 3385-21-5, 1,3-Diaminocyclohexane 3619-73-6 3731-51-9, 2-(Aminomethyl)pyridine 3731-53-1, 4-Aminomethylpyridine 3973-70-4, 1-Amino-4-(2-hydroxyethyl)piperazine 4023-34-1, Cyclopropanecarbonyl chloride 4318-37-0, 1-Methylhomopiperazine 4319-49-7, N-Aminomorpholine 4403-71-8, 4-Aminobenzylamine 4524-93-0, Cyclopentanecarbonyl chloride 4693-91-8, 4-Methoxyphenylacetyl chloride 4897-50-1, 4-Piperidinopiperidine 5004-07-9, 4-Pyrrolidinopiperidine 5006-22-4, Cyclobutanecarbonyl chloride 5036-48-6, 1-(3-Aminopropyl)imidazole 5308-25-8, 1-Ethylpiperazine 5382-16-1, 4-Hydroxypiperidine 5657-70-5, 1-Methylpiperidine-3-carboxylic acid 6457-49-4, 4-(Hydroxymethyl)piperidine 6834-42-0, 3-Methoxyphenylacetyl chloride 6859-99-0, 3-Hydroxypiperidine 6928-85-4 7144-05-0, 4-Aminomethylpiperidine 7154-73-6, 1-(2-Aminoethyl)pyrrolidine 7663-77-6, 1-(3-Aminopropyl)-2-pyrrolidinone 7693-46-1, 4-Nitrophenyl chloroformate 10313-60-7, 3,4-Dimethoxyphenylacetyl chloride 10342-85-5 13035-19-3, 4-Aminopiperidine 13365-26-9, Dimethyl 3-nitrophthalate 14777-27-6, Methyl acetimidate hydrochloride 16596-41-1, 1-Aminopyrrolidine 17078-28-3, 4-(Dimethylamino)phenylacetic acid 20173-24-4, 3-(2-Aminoethyl)pyridine 23356-96-9, (S)-2-(Hydroxymethyl)pyrrolidine 24424-99-5, Di-tert-butyl dicarbonate 25026-34-0, 4-Chlorophenylacetyl chloride 27219-07-4, 5-(tert-Butoxycarbonylamino)valeric acid 27578-60-5, 1-(2-Aminoethyl)piperidine 30923-69-4 34803-66-2 36268-42-5 37920-25-5 38205-60-6, 2,4-Dimethyl-5-acetylthiazole 39135-39-2, 1-Amino-2,6-dimethylpiperidine 39546-32-2, Isonipecotamide 39910-98-0

50533-97-6, 4-Dimethylaminopiperidine 50534-49-1 51387-90-7, 2-(2-Aminoethyl)-1-methylpyrrolidine 51512-09-5, 2-Chlorophenylacetyl chloride 51639-48-6 52513-35-6 52659-18-4, Dimethyl 3-acetamidophthalate 52711-92-9, 2,5-Dimethoxyphenylacetyl chloride 54012-73-6, 3-Aminopiperidine 57184-25-5, 1-(Cyclopropylmethyl)piperazine 57260-71-6 57294-38-9, 4-(tert-Butoxycarbonylamino)butyric acid 59983-39-0 60419-23-0 60717-51-3, 2-(Dimethylaminomethyl)piperidine 64021-83-6 64030-44-0, (S)-2-(Phenylaminomethyl)pyrrolidine 64168-09-8, 2-(Diethylaminomethyl)piperidine 66493-39-8, 4-(tert-Butoxycarbonylamino)benzoic acid 67990-65-2 68947-43-3, 1-Methylpiperidine-4-carboxylic acid 69478-75-7 72748-99-3, (R)-1-Amino-2-(methoxymethyl)pyrrolidine 73579-08-5, 1-Methyl-4-(methylamino)piperidine 73873-59-3 73873-61-7 76513-69-4, 2-(Trimethylsilyl)ethoxymethyl chloride 78771-35-4 79286-79-6, 3-Aminopyrrolidine 81196-09-0, 4-(tert-Butoxycarbonylamino)phenylacetic acid 84025-81-0, (R)-2-(Methoxymethyl)pyrrolidine 84358-12-3, 1-tert-Butoxycarbonylpiperidine-3-carboxylic acid 84358-13-4, 1-(tert-Butoxycarbonyl)piperidine-4-carboxylic acid 87120-72-7, 4-Amino-1-(tert-butoxycarbonyl)piperidine 89855-60-7 89895-06-7, 4-Acetylpiperidine hydrochloride 112275-50-0, 1-tert-Butoxycarbonylhomopiperazine 118430-74-3 118535-61-8 120570-05-0, (S)-(-)-3-Aminoquinuclidine 121224-35-9 127221-89-0 130309-46-5 132339-20-9, (1S,4S)-(+)-2,5-Diazabicyclo[2.2.1]heptane 132883-44-4 132958-72-6 134679-22-4 134868-23-8, 4-(Dimethylamino)cyclohexanecarboxylic acid 139015-32-0 162755-96-6 165328-10-9 247150-03-4 309962-63-8 347186-01-0 360793-02-8 364734-27-0 364734-39-4 364734-41-8 364734-86-1 364734-89-4 364734-92-9 364734-94-1 364734-97-4 364734-99-6 364735-04-6 364735-08-0 364735-33-1 364735-52-4 364735-65-9 364735-68-2
(reactant; preparation of indeno[c]pyrazolones as inhibitors of cyclin dependent kinases)

IT 3385-21-5, 1,3-Diaminocyclohexane
(reactant; preparation of indeno[c]pyrazolones as inhibitors of cyclin dependent kinases)

RN 3385-21-5 USPATFULL

CN 1,3-Cyclohexanediamine (CA INDEX NAME)



L79 ANSWER 33 OF 38 USPATFULL on STN

ACCESSION NUMBER: 2001:209008 USPATFULL Full-text

TITLE: Quinolones used as MRS inhibitors and bactericides

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PATENT INFORMATION:	US 6320051	B1	20011120		<--
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PRIORITY INFORMATION:	GB 1998-9050	19980429	<--
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LEGAL REPRESENTATIVE: Hall, Linda E., Venetianer, Stephen A., Kinzig, Charles M.
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
LINE COUNT: 2643
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB ##STR1##

Compounds of formula (I) are inhibitors of the bacterial enzyme S aureus methionyl tRNA synthetase and are of use in treating bacterial infections.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AI 19990415
20001026 PCT 371 date
20001026 PCT 102(e) date
SUMM 2-[3-(2,3,5-Trichlorobenzylamino)prop-1-ylamino]-1H-quinolin-4-one dihydrochloride;
SUMM 2-[3-(3,5-Dibromo-2-ethoxybenzylamino)prop-1-ylamino]-1H-quinolin-4-one dihydrochloride;
DETD b) 2-(3-Aminoprop-1-ylamino)-1H-quinolin-4-one dihydrochloride
DETD 2-[3-(3,4-Dichlorobenzylamino)prop-1-ylamino]-1H-quinolin-4-one hydrochloride
DETD . . . acid (40 mg, 0.167 mmol), 1-hydroxy-7-azabenzotriazole (23 mg, 0.167 mmol), and diethylaminomethyl-polystyrene (152 mg, 0.456 mmol). After 15 min 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride (32 mg, 0.167 mmol) was added to the stirred mixture. The polystyrene was removed by filtration after 24 h and. . .
DETD . . . acid (35 mg, 0.183 mmol), 1-hydroxy-7-azabenzotriazole (25 mg, 0.183 mmol), and diethylaminomethyl-polystyrene (166 mg, 0.498 mmol). After 15 min 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride (35 mg, 0.183 mmol) was added to the stirred mixture. The polystyrene was removed by filtration after 19 h and. . .
DETD a) 2-(2-Aminoethylamino)-1H-quinolin-4-one dihydrochloride
DETD . . . 0.2 mmol), diethylaminomethylpolystyrene (0.22 g, 0.66 mmol), 5,6-dichloronicotinic acid (0.042 g, 0.22 mmol), 1-hydroxy-7-azabenzotriazole (0.030 g, 0.22 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.042 g, 0.22 mmol) in DMF (2.5 ml) were stirred under argon at room temperature for 18 h. The mixture. . .
DETD a) 2-(4-Aminobut-1-ylamino)-1H-quinolin-4-one dihydrochloride
DETD b) 2-(3-amino-2,2-dimethylprop-1-ylamino)quinolin-4-one dihydrochloride

DETD . . . was added to a stirred mixture of compound 27b (0.040 g, 0.113 mmol), 3,4-dichlorobenzoic acid (0.022 g, 0.113 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodimide hydrochloride (0.043 g, 0.225 mmol) and 1-hydroxy-7-azabenzotriazole (0.031 g, 0.225 mmol) in DMF (4 ml) at room temperature and under argon,. . .

DETD b) 2-(cis-3-Aminocyclohexylamino)-1H-quinolin-4-one dihydrochloride

DETD b) 2-(5-Aminopent-1-ylamino)-1H-quinolin-4-one dihydrochloride

DETD . . . procedure to that described in example 24 from compound 30b (0.07 g, 0.22 mmol), 1-hydroxy-7-azabenzotriazole (0.03 g, 0.22 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.05 g, 0.26 mmol), 3,4-dichlorobenzoic acid (0.042 g, 0.22 mmol) and diisopropylethylamine (0.115 ml, 0.66 mmol) in dry DMF (2. . .

DETD c) 2-[2-(Aminomethyl)pent-1-ylamino]-1H-quinolin-4-one dihydrochloride

DETD 2-[3-(2,3,5-Trichliorobenzylamino)prop-1-ylamino]-1H-quinolin-4-one dihydrochloride

DETD 2-[3-(3,5-Dibromo-2-ethoxybenzylamino)prop-1-ylamino]-1H-quinolin-4-one dihydrochloride

DETD b) 2-(2-Aminomethylallylamino)-1H-quinolin-4-one dihydrochloride

DETD The title compound was prepared according to the method described in Example 23(b) from 2-(2-aminomethylallylamino)-1H-quinolin-4-one dihydrochloride (85 mg, 0.28 mmol), 3,4-dichlorobenzaldehyde (50 mg, 0.29 mmol), sodium acetate (47 mg, 0.58 mmol) and sodium cyanoborohydride (18 mg,. . .

DETD d) 2-[(2-aminocyclopentyl)methylamino]-1H-quinolin-4-one dihydrochloride

DETD A suspension of 2-[(2-aminocyclopentyl)methylamino]-1H-quinolin-4-one dihydrochloride (0.040 g, 0.121 mmol), sodium acetate (0.025 g, 0.303 mmol) and 3,4-dichlorobenzaldehyde (0.021 g, 0.121 mmol) in 1% acetic acid. . .

DETD c) 2-(3-amino-2-methoxyprop-1-ylamino)quinolin-4-one dihydrochloride

DETD A suspension of 2-(3-amino-2-methoxyprop-1-ylamino)quinolin-4-one dihydrochloride (0.15 g, 0.468 mmol), sodium acetate (0.096 g, 1.17 mmol) and 3,4-dichlorobenzaldehyde (0.082 g, 0.468 mmol) in 1% acetic acid. . .

DETD 2-[3-(3,4-Dichlorobenzylamino)prop-1-ylamino]-6-methyl-1H-quinolin-4-one dihydrochloride

DETD e) 2-[3-(3,4-Dichlorobenzylamino)prop-1-ylamino]-6-methyl-1H-quinolin-4-one dihydrochloride

DETD 2-[3-(3,4-Dichlorobenzylamino)prop-1-ylamino]-5-chloro-1H-quinolin-4-one dihydrochloride

DETD d) 2-[3-(3,4-Dichlorobenzylamino)prop-1-ylamino]-5-chloro-1H-quinolin-4-one dihydrochloride

DETD e. 2-[((1R,2R)-2-Aminocyclopentylmethyl)amino]-1H-quinolin-4-one dihydrochloride

DETD The title compound was prepared from 2-[((1R,2R)-2-aminocyclopentylmethyl)amino]-1H-quinolin-4-one dihydrochloride(0.059 g, 0.18 mmol), 3,4-dichlorobenzaldehyde (0.031 g, 0.18 mmol), sodium acetate (0.045 g, 0.54 mmol) and sodium cyanoborohydride (0.02 g, 0.32. . .

DETD c. 2-[((1R,2S)-2-Aminocyclopentylmethyl)amino]-1H-quinolin-4-one dihydrochloride

DETD . . . using sodium acetate (0.020 g, 0.242 mmol), sodium cyanoborohydride (0.012 g, 0.194 mmol), 3,4-dichlorobenzaldehyde (0.017 g, 0.0969 mmol), and 2-[((1R,2S)-2-aminocyclopentylmethyl)amino]-1H-quinolin-4-one dihydrochloride (0.032 g, 0.0969 mmol). δ.sub.H (CD.sub.3 OD) 1.25-2.05 (7H, m), 2.73-2.81 (1H, m), 3.10-3.29 (2H, m), 3.61-3.80 (2H, m), 5.56. . .

CLM What is claimed is:

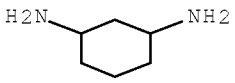
. . . from: 2-[3-(3-Quinolinylmethylamino)prop-1-ylamino]-1H-quinolin-4-one; 2-[3-(2-Naphthylmethylamino)prop-1-ylamino]-1H-quinolin-4-one; 2-[3-(2-Naphthylmethyl(acetyl)amino)prop-1-ylamino]-1H-quinolin-4-one;

2-[3-(2-Trifluoromethylbenzylamino)prop-1-ylamino]-1H-quinolin-4-one;
2-[3-(4-Chloro-3-sulfamoylbenzylamino)prop-1-ylamino]-1H-quinolin-4-one;
2-[3-(2-Benzyloxybenzylamino)prop-1-ylamino]-1H-quinolin-4-one;
2-[3-(3-Chlorobenzylamino)prop-1-ylamino]-1H-quinolin-4-one and;
2-{3-[bis(3-Chlorobenzyl)amino]prop-1-ylamino}-1H-quinolin-4-one;
2-[3-(3-Chloro-4-fluorobenzylamino)prop-1-ylamino]-1H-quinolin-4-one;
2-{3-[1-(3,4-Dichlorophenyl)ethylamino]prop-1-ylamino}-1H-quinolin-4-one;
2-{3-[3,4-Dichlorophenyl(phenyl)methylamino]prop-1-ylamino}-1H-quinolin-4-one; 2-[3-(4-Fluorobenzylamino)prop-1-ylamino]-1H-quinolin-4-one;
2-[3-(Benzofuran-2-ylmethylamino)prop-1-ylamino]-1H-quinolin-4-one;
2-[3-(Cinnamylamino)prop-1-ylamino]-1H-quinolin-4-one;
2-[3-(2-Methoxycinnamylamino)prop-1-ylamino]-1H-quinolin-4-one;
2-(3-(4-Methoxycinnamylamino)prop-1-ylamino]-1H-quinolin-4-one
2-{3-[bis(4-Methoxycinnamyl)amino]prop-1-ylamino}-1H-quinolin-4-one;
2-[3-(3,4-Dichlorobenzylamino)prop-1-ylamino]-1H-quinolin-4-one hydrochloride; 2-[3-(4-Cyanobenzylamino)prop-1-ylamino]-1H-quinolin-4-one; 2-{3-[N-(3,4-Dichlorobenzyl)-N-prop-2-ylamino]prop-1-ylamino}-1H-quinolin-4-one; 2-[3-(5-Bromoindole-2-carboxamido)prop-1-ylamino]-1H-quinolin-4-one; 2-[3-(5,6-Dichloronicotinoylamino)prop-1-ylamino]-1H-quinolin-4-one; 2-[2-(3,4-Dichlorobenzylamino)ethylamino]-1H-quinolin-4-one; 2-[2-(5,6-Dichloronicotinoylamino)ethylamino]-1H-quinolin-4-one;
2-[2-(3-Benzoylbenzoylamino)ethylamino]-1H-quinolin-4-one;
2-[4-(3,4-Dichlorobenzylamino)but-1-ylamino]-1H-quinolin-4-one;
2-[3-(3,4-Dichlorobenzylamino)-2,2-dimethylprop-1-ylamino]-1H-quinolin-4-one; 2-[3-(3,4-Dichlorobenzoylamino)-2,2-dimethylprop-1-ylamino]-1H-quinolin-4-one; 2-[cis-3-(3,4-Dichlorobenzylamino)cyclohexylamino]-1H-quinolin-4-one; 2-[5-(3,4-Dichlorobenzylamino)pent-1-ylamino]-1H-quinolin-4-one; 2-[5-(3,4-dichlorobenzoylamino)pent-1-ylamino]-1H-quinolin-4-one; 2-[3-(3,4-Dichlorobenzylamino)propyloxy]-1H-quinolin-4-one bis(trifluoroacetate); 2-{2-[(3,4-Dichlorobenzylamino)methyl]pent-1-ylamino]-1H-quinolin-4-one; 2-[3-(3,5-Dichlorobenzylamino)prop-1-ylamino]-1H-quinolin-4-one; 2-[3-(3-Iodobenzylamino)prop-1-ylamino]-1H-quinolin-4-one; 2-[3-(3,5-Diiodobenzylamino)prop-1-ylamino]-1H-quinolin-4-one; 2-[3-(4,5-Dibromothienylamino)prop-1-ylamino]-1H-quinolin-4-one;
2-[3-(4-Chloro-3-trifluoromethylbenzylamino)prop-1-ylamino]-1H-quinolin-4-one; 2-[3-(2-Benzyloxy-3,5-dichlorobenzylamino)prop-1-ylamino]-1H-quinolin-4-one; 2-[3-(3,5-Dibromobenzylamino)prop-1-ylamino]-1H-quinolin-4-one; 2-[3-(3,5-Dibromo-4-methylbenzylamino)prop-1-ylamino]-1H-quinolin-4-one; 2-[3-(3,4,5-Tribromobenzylamino)prop-1-ylamino]-1H-quinolin-4-one;
2-[3-(3-Bromo-5-iodobenzylamino)prop-1-ylamino]-1H-quinolin-4-one;
2-{3-[N-(3,4-Dichlorobenzyl)-N-methylamino]prop-1-ylamino}-1H-quinolin-4-one; 2-[3-(2,3,5-Trichlorobenzylamino)prop-1-ylamino]-1H-quinolin-4-one dihydrochloride; 2-[3-(3,5-Dibromo-2-ethoxybenzylamino)prop-1-ylamino]-1H-quinolin-4-one dihydrochloride; 2-[3-(1,3-Dichloro-5,6-dihydro-4H-cyclopenta[c]thiophen-4-ylamino]prop-1-ylamino}-1H-quinolin-4-one;
2-[3-(5,7-Dimethyl-1,2,3,4-tetrahydro-naphthalen-1-ylamino)prop-1-ylamino]-1H-quinolin-4-one; 2-[2-(2-(3,4-Dichlorophenyl)ethylamino)ethylamino]-1H-quinolin-4-one; 2-[3-(2-(3,4-Dichlorophenyl)ethylamino)prop-1-ylamino]-1H-quinolin-4-one; 2-[3-(5,7-Dichloro-1,2,3,4-tetrahydronaphth-1-ylamino)prop-1-ylamino]-1H-quinolin-4-one; 2-[3-(4,6-Dichloro-3-methylindan-1-ylamino)prop-1-ylamino]-1H-quinolin-4-one;
2-[3-(5,6,7-Trichloro-1,2,3,4-tetrahydronaphth-1-ylamino)prop-1-ylamino]-1H-quinolin-4-one; 2-[3-(5,6,7-Trichloro-3-methylindan-1-ylamino)prop-1-ylamino]-1H-quinolin-4-one; 2-[3-(4,6-Dichloroindan-1-ylamino)prop-1-ylamino]-1H-quinolin-4-one; 2-{3-[2-(3,4-Dichlorophenyl)azetidin-1-yl]prop-1-ylamino}-1H-quinolin-4-one; 2-{3-[(4,5-Dibromofur-2-ylmethyl)amino]prop-1-ylamino}-1H-quinolin-4-one; 2-{2-[(3,4-Dichlorobenzylamino)methyl]allylamino}-1H-quinolin-4-one;
2-{[1-(3,4-Dichlorobenzyl)piperidin-2-ylethyl]amino}-1H-quinolin-4-one;
2-{[2-(3,4-Dichlorobenzylamino)cyclopentyl]methylamino}-1H-quinolin-4-

one; 2-[3-(3,4-Dichlorobenzylamino)-2-methoxyprop-1-ylamino]-1H-quinolin-4-one; 2-[3-(3,4-Dichlorobenzylamino)prop-1-ylamino]-6-methyl-1H-quinolin-4-one dihydrochloride; 2-[3-(3,4-Dichlorobenzylamino)prop-1-ylamino]-5-chloro-1H-quinolin-4-one dihydrochloride; 2-[3-(2,3,4,9-Tetrahydro-1H-carbazol-1-ylamino)prop-1-ylamino]-1H-quinolin-4-one; 2-{3-[(3,4,5-Tribromothiophen-2-ylmethyl)amino)prop-1-ylamino]-1H-quinolin-4-one; 2-{3-[(3,4-Dibromo-5-methyl-1H-pyrrol-2-ylmethyl)amino)prop-1-ylamino]-1H-quinolin-4-one; 2-[3-(2-tert-Butoxycarbonylmethoxy-3,5-dichlorobenzylamino)prop-1-ylamino]-1H-quinolin-4-one, 2-[3-(2-Allyloxy-3,5-dichlorobenzylamino)prop-1-ylamino]-1H-quinolin-4-one; 2-[3-(3,5-Dichloro-2-phenethoxybenzylamino)propylamino]-1H-quinolin-4-one; 2-{[(1R,2R)-2-(3,4-Dichlorobenzylamino)cyclopentylmethyl]amino}-1H-quinolin-4-one; 2-{[(1R,2S)-2-(3,4-Dichlorobenzylamino)cyclopentylmethyl]amino}-1H-quinolin-4-one; 2-{[(1S,2S)-2-(3,4-Dichlorobenzylamino)cyclopentylmethyl]amino}-1H-quinolin-4-one; 2-{[(1R,2S)-2-(3,5-Dibromobenzylamino)cyclopentylmethyl]amino}-1H-quinolin-4-one; 2-{[(1R,2S)-2-(4,5-Dibromo-2-thiophenemethylamino)cyclopentylmethyl]amino}-1H-quinolin-4-one; 2-{[(1R,2S)-2-(3,5-Dibromo-2-ethoxybenzylamino)cyclopentylmethyl]amino}-1H-quinolin-4-one; 2-[3-(4,6-Dichloroindol-2-ylmethylamino)prop-1-ylamino]-1H-quinolin-4-one; and 2-[3-(2-Amino-3,5-dibromobenzylamino)prop-1-ylamino]-1H-quinolin-4-one.

IT 51-44-5, 3,4-Dichlorobenzoic acid 66-99-9, Naphthalene-2-carboxaldehyde 67-64-1, 2-Propanone, reactions 87-61-6, 1,2,3-Trichlorobenzene 90-60-8, 3,5-Dichlorosalicylaldehyde 96-48-0 102-47-6, 3,4-Dichlorobenzyl chloride 103-63-9, (2-Bromoethyl)benzene 105-07-7, 4-Cyanobenzaldehyde 106-49-0, 4-Methylaniline, reactions 107-15-3, 1,2-Ethanediamine, reactions 108-42-9, 3-Chloroaniline 109-76-2, 1,3-Diaminopropane 110-60-1, 1,4-Butanediamine 141-82-2, Malonic acid, reactions 156-87-6 447-61-0, 2-Trifluoromethylbenzaldehyde 459-57-4, 4-Fluorobenzaldehyde 462-94-2, 1,5-Diaminopentane 541-73-1, 1,3-Dichlorobenzene 579-18-0, 3-Benzoylbenzoic acid 587-04-2, 3-Chlorobenzaldehyde 696-41-3, 3-Iodobenzaldehyde 703-61-7, 2,4-Dichloroquinoline 1189-71-5, Chlorosulfonyl isocyanate 2039-83-0, 3,4-Dichlorostyrene 2433-85-4, 4,5-Dibromofuran-2-carboxaldehyde 2642-63-9 2706-56-1, 2-Pyridineethanamine 3279-81-0, 4-Chloro-3-sulfamoylbenzaldehyde 3385-21-5, 1,3-Diaminocyclohexane 3456-99-3 4265-16-1, Benzofuran-2-carboxaldehyde 4295-08-3, 2-Chloro-4-ethoxyquinoline 4295-09-4, 2-Chloro-4-methoxyquinoline 5896-17-3, 2-Benzyloxybenzaldehyde 6284-79-3, 3,4-Dichlorobenzophenone 6287-38-3, 3,4-Dichlorobenzaldehyde 7254-19-5, 5-Bromoindole-2-carboxylic acid 7687-79-8 10203-08-4, 3,5-Dichlorobenzaldehyde 10465-81-3 13669-42-6, Quinoline-3-carboxaldehyde 14371-10-9, trans-Cinnamaldehyde 17352-25-9, 3,5-Diiodobenzaldehyde 18880-04-1, 3,4-Dichlorobenzyl bromide 22031-52-3, 6-Azabicyclo[3.2.0]heptan-7-one 24680-50-0 34328-46-6, 4-Chloro-3-trifluoromethylbenzaldehyde 34328-61-5, 3-Chloro-4-fluorobenzaldehyde 38071-22-6, 4,5-Dibromothiophene-2-carboxaldehyde 38091-73-5 40359-57-7, 2-Benzyloxy-3,5-dichlorobenzaldehyde 41365-75-7 41667-95-2, 5,6-Dichloronicotinic acid 50910-55-9, 2-Amino-3,5-dibromobenzaldehyde 52176-31-5, 2-Amino-4-ethoxyquinoline 53995-82-7 55144-92-8, 3-(2,4-Dichlorophenyl)propanoic acid 56123-06-9, 2-Methylenepropane-1,3-diamine 56961-75-2, 2,3,5-Trichlorobenzaldehyde 56990-02-4, 3,5-Dibromobenzaldehyde 60125-24-8, trans-2-Methoxycinnamaldehyde 61657-67-8, 3,5-Dibromo-2-ethoxybenzaldehyde 74896-66-5 93467-56-2 102000-64-6 149877-00-9 151379-87-2 158414-41-6 181280-06-8 248607-95-6 248607-96-7 248607-97-8
(preparation of 2-aminoquinolin-4-ones as inhibitors of methionyl tRNA

synthase)
IT 3385-21-5, 1,3-Diaminocyclohexane
(preparation of 2-aminoquinolin-4-ones as inhibitors of methionyl tRNA synthase)
RN 3385-21-5 USPATFULL
CN 1,3-Cyclohexanediamine (CA INDEX NAME)



L79 ANSWER 34 OF 38 USPATFULL on STN

ACCESSION NUMBER:	2000:1995 USPATFULL Full-text		
TITLE:	Synthesis of macrocyclic tetraamido-N ligands		
INVENTOR(S):	Gordon-Wylie, Scott W., Pittsburgh, PA, United States Collins, Terrence J., Pittsburgh, PA, United States		
PATENT ASSIGNEE(S):	Carnegie Mellon University, Pittsburgh, PA, United States (U.S. corporation)		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6011152		20000104 <--
APPLICATION INFO.:	US 1998-158487		19980922 (9) <--
RELATED APPLN. INFO.:	Division of Ser. No. US 1996-681187, filed on 22 Jul 1996		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Shah, Mukund J.		
ASSISTANT EXAMINER:	Sripada, Pavanaram K		
LEGAL REPRESENTATIVE:	Kirkpatrick & Lockhart LLP		
NUMBER OF CLAIMS:	28		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	5 Drawing Figure(s); 3 Drawing Page(s)		
LINE COUNT:	2451		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB New synthetic methods for the preparation of macrocyclic amido-N donor ligands are provided. The primary method of the present invention involves in general only two synthetic steps. In the first step, an α or β amino carboxylic acid is allowed to react with an optimal (approximately stoichiometric) amount of an activated malonate or oxalate derivative with mild heating. Upon completion of the double coupling reaction, hydrolysis of the reaction mixture yields a diamide containing intermediate (a macro linker). In the second step, stoichiometric amounts of a diamine, preferably an orthophenylene diamine, are added to the macro linker intermediate in the presence of a coupling agent and heat. This second double coupling reaction, is allowed to proceed for a period of time sufficient to produce a macrocyclic tetraamido compound. The substituent groups on the α or β amino carboxylic acid, the malonate, and the aryl diamine may all be selectively varied so that the resulting tetraamido macrocycle can be tailored to specific desired end uses. The macrocyclic tetraamide ligand may then be complexed with a metal, such as a transition metal, and preferably the middle and later transition metals, to form a robust chelate complex suitable for catalyzing oxidation reactions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . (L-α-amino-β-
phenyl citrulline
propionic acid) (L-2-amino-5-ureidovaleric acid)

Other Amino Acids Other Amino Acids

(S)-2-amino-3-methoxypropionic acid α-aminohydrocinnamonitrile
α-amino-β-methyl'aminopropionic acid
L-2-amino-4-hydroxy butyric acid
hydrochloride (R,S)-2-amino-3-hydroxy-3-methyl
R(-)-2-amino-2-methyl butanedioic butanoic acid
acid (2S,3R)-2-amino-3-hydroxy-4-methyl
S(+)-2-amino-2-methyl butanedioic pentanoic acid
acid DL-α-amino-β-hydroxy-valeric acid
S(+)-2-amino-2-methyl butanoic acid α-amino-β-imidazole
propionic acid
. . . anthranilic acid) anthranilic acid)
619-17-0 4-nitro- 3177-80-8 3-methoxy-
616-79-5 5-nitro- 6705-03-9 5-methoxy-
4389-45-1 3-methyl- 394-31-0 5-hydroxy-
2305-36-4 4-methyl- 4920-81-4 3-hydroxy- hydrochloride
2941-78-8 5-methyl- 446-32-2 4-fluoro-
4389-50-8 6-methyl- 446-08-2 5-fluoro-
609-86-9 3,5-diiodo- 434-76-4 6-fluoro-
5653-40-7 4,5-dimethoxy- 4-chloro-5-sulfanoyl-
50419-58-4 3,4-dimethyl- 6388-47-2 3-chloro-
14438-32-5. . . # carboxylic acids

3-amino-5-phenylthiophene- 5959-52-4 3-amino-2-napthoic acid
carboxamide 5345-47-1 2-amino-nicotinic acid (2-
5434-20-8 3-amino-pthalic acid aminopyridine-3-carboxylic
627-95-2 b-amino-valeric acid acid)
hydrochloride 82-24-6 1-amino-anthraquinone-2-
2-amino-4-methyl- carboxylic acid
thiophene-3-carboxamide 1664-54-6 3-amino-3-phenyl-propionic
2-amino-5-methyl- acid
thiophene-3-carboxamide 50427-77-5 5-amino-1-phenylpyrazole-
1068-84-4 amino-malonic acid 4-carboxamide
614-19-7 β-amino-hydrocinnamic acid 72-40-2 5(4)-aminoimidazole-4(5
)-
(D,L-3-amino-3-phenyl- carboxamide hydrochloride
propionic acid) 2627-69-2 5-amino-4-imidazole
4507-13-5 2-amino-5-ethylthiophene- carboxamide riboside
3-carboxylic acid, ethyl 68302-09-0 2-amino-7-ethyl-5-oxo-5H-
ester [1]benzopyrano[2,3-
52834-01-2 2-amino-4,6-dimethyl-3- b]pyridine-3-carbonitrile
pyridinecarboxylic acid 22603-53-8 2-amino-3,5-
hydrochloride dinitrobenzonitrile
54711-21-6 5-amino-4-cyano-1-methyl- 5-amino-4-cyano-1-(4-
pyrazole chlorophenyl)pyrazole
698-29-3 4-amino-5-cyano-2-methyl 5-amino-4-cyano-1-(4-
pyrimidine nitrophenyl) pyrazole
4-amino-5-cyano-2-methoxy 16617-46-2 5-amino-4-cyano pyrazole
pyrimidine 21112-45-8 β-amino-crotonic acid
. . .
DETD . . . acid
Derivatives of n,n+2 Diamines (6aa)

Registry #
n,n+2-diamines
Registry #
n,n+2-diamines

4403-69-4 2-amino-benzylamine 2,4-diamino-2,4-dimethyl-
2-amino-2-(2-aminophenyl)- pentane-3-one
propane 2,4-diamino-2,4-dimethyl-
109-76-2 1,3-diaminopropane pentane
3385-21-5 1,3-diaminocyclohexane 479-27-6 1,8-diaminonapthalene
1,3-diamino-1,3- 589-37-7 1,3-diaminopentane
dimethylcyclohexane 7328-91-8 1,3-diamino-2,2-
dimethyl
propane

DETD . . . to 1,2-Diamino-4-acetamidobenzene in acetic acid (HOAc)/MeOH using catalytic hydrogenation over a 10% Pd/C catalyst. The material was isolated as the dihydrochloride salt. Yield >90%. Characterization: .sup.1 H NMR (CD.sub.3 OD) δ [ppm]: 6.94 (m, 1 H, ArH), 6.68 (m, 1 H,. . . solvate HCl/H.sub.2 O was confirmed by IR, and is consistent with the constant boiling 36.5-38% HCl used to generate the hydrochloride salt.

DETD . . . collected from washings that have been pooled from several different preparations. The product must be stored as the dihydrobromide or dihydrochloride salt to protect the amines from oxidative degradation. Characterization: .sup.1 H NMR (CDCl.sub.3 /DMSO-d.sup.6) of 2,4-diamino-2,4-dimethyl-pentan-3-one. 2 HBr: 8.62 (6H,. . .

DETD . . . formation of an unfavorable hydrogen bond, the ring closure reaction requires lengthy reflux times in order to achieve macrocyclization. 1,2-Diamino-4-acetamidobenzene dihydrochloride (9 mmol) was employed as the diamine in an oxazalone ring closure reaction. The macrocyclization time was increased (reflux, 5. . .

L79 ANSWER 35 OF 38 USPATFULL on STN
ACCESSION NUMBER: 1998:36764 USPATFULL Full-text
TITLE: N,N-bis (quinolin-4-yl)-diamine derivatives, their preparation and their use as antimalarials
INVENTOR(S): Hofheinz, Werner, Bottmingen, Switzerland
Leupin, Werner, Liestal, Switzerland
PATENT ASSIGNEE(S): Hoffman-La Roche, Inc., Nutley, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 5736557		19980407		<--
	WO 9535287		19951228		<--
APPLICATION INFO.:	US 1996-765751		19961216	(8)	<--
	WO 1995-EP2123		19950603		<--
			19961216	PCT 371 date	
			19961216	PCT 102(e) date	

	NUMBER	DATE	
PRIORITY INFORMATION:	CH 1994-1928	19940617	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Ivy, C. Warren
ASSISTANT EXAMINER: Huang, Evelyn
LEGAL REPRESENTATIVE: Johnston, George W., Rocha-Tramaloni, Patricia S.
NUMBER OF CLAIMS: 10

EXEMPLARY CLAIM: 1
LINE COUNT: 689
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are N,N'-bis(quinolin-4-yl)diamine derivatives of general formula I wherein R.sup.1 signifies halogen or trifluoromethyl, R.sup.2 signifies hydrogen or halogen, A signifies cyclohexane-1,3-diyl, 2-methyl-cyclohexane-1,3-diyl, cyclohexane-1,4-diyl, dicyclohexylmethane-4,4'-diyl, cyclopentane-1,3-diyl, phenylene-1,4, phenylene-1,3 and phenylene-1,2; n is 1 or 2; m is 1 or 2, as well as their pharmaceutically acceptable salts. These products are useful as agents for preventing malaria and for treating it, especially where the pathogens are resistant to chloroquine. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AI 19950603
19961216 PCT 371 date
19961216 PCT 102(e) date

DETD 2.67 g of 4,7-dichloroquinoline, 1.47 g of α,α'-diamino-o-xylene dihydrochloride and 3.8 ml of triethylamine are reacted at 140° C. under argon for 5 hours. After cooling 100 ml of. . .

DETD . . . HCl and brought into solution on a steam bath by the addition of ethanol (75 ml). 3.14 g of the dihydrochloride crystallize out upon cooling, m.p.:>250° C.

DETD . . . with the addition of 100 ml of ethyl acetate, 0.8 g of crystalline amine being obtained. 0.84 g of crystalline dihydrochloride, m.p.:>250° C., is obtained therefrom by boiling in 15 ml of 1N HCl and 10 ml of ethanol.

DETD . . . to Example 3, from 2.28 g of ±trans-cyclohexane-1,4-diamine and 7.92 g of 4,7-dichloroquinoline there are obtained 2 g of the dihydrochloride; colourless crystals from methanol-water, m.p.:>250° C.

DETD The dihydrochloride, colourless crystals from methanol-water, m.p.:>260° C., is obtained analogously to Example 3 from cis-cyclohexane-1,4-diamine and 4,7-dichloroquinoline.

DETD . . . of 4,7-dichloroquinoline there are obtained 1.6 g of pure diamine. This is dissolved in 16 ml of hot isopropanol. The dihydrochloride crystallizes out after the addition of 1.6 ml of 4.8N isopropanolic hydrochloric acid. 1.04 g of colourless crystallizate are obtained,. . .

DETD Analogously to Example 3, from 3.36 of cis,cis-2-methyl-cyclohexane-1,3-diamine dihydrochloride, 10.38 g of 4,7-dichloroquinoline and 5.3 g of triethylamine there are obtained 1.23 g of pure diamine. From a hot. . .

DETD 6.3 g of colourless, crystalline dihydrochloride, m.p.:>250° C., are obtained from 4.2 g of 4,4'-diaminodicyclohexylmethane and 7.92 g of 4,7-dichloroquinoline.

DETD In analogy to Example 6, from 1.6 g of trans-2-butene-1,4-diamine dihydrochloride, 4 g of 4,7-dichloroquinoline and 4 g of triethylamine there are obtained 1.5 g of the base. This is converted. . .

DETD . . . methylene chloride. After evaporation of the solvent the residue as is taken up in 25 ml of isopropanol and the dihydrochloride of the product is crystallized with 20 ml of 3.26N isopropanolic hydrochloric acid. There are obtained 2.64 g, colourless crystals;. . .

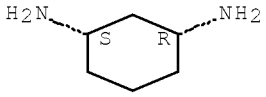
IT 17300-02-6P, α,α'-Diamino-o-xylene 21294-14-4P, α,α'-Diamino-o-xylene dihydrochloride 26772-34-9P, cis-Cyclohexane-1,3-diamine 26883-70-5P, trans-Cyclohexane-1,3-diamine 59255-77-5P 63486-45-3P, cis-Cyclopentane-1,3-diamine 95213-40-4P 174893-22-2P 174893-23-3P 174893-24-4P,

trans-Cyclohexane-1,3-diamine bistrifluoroacetate 174893-25-5P,
cis-Cyclopentane-1,3-diamine dihydrobromide 175131-75-6P,
cis,cis-2-Methylcyclohexane-1,3-diamine 175271-22-4P
(intermediate; preparation of bis(quinolinyl)diamine derivs. as antimalarials)

IT 26772-34-9P, cis-Cyclohexane-1,3-diamine 26883-70-5P,
trans-Cyclohexane-1,3-diamine
(intermediate; preparation of bis(quinolinyl)diamine derivs. as antimalarials)

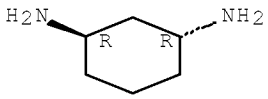
RN 26772-34-9 USPATFULL
CN 1,3-Cyclohexanediamine, (1R,3S)-rel- (CA INDEX NAME)

Relative stereochemistry.



RN 26883-70-5 USPATFULL
CN 1,3-Cyclohexanediamine, (1R,3R)-rel- (CA INDEX NAME)

Relative stereochemistry.

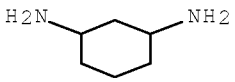


L79 ANSWER 36 OF 38 USPATFULL on STN

ACCESSION NUMBER:	91:66932 USPATFULL Full-text			
TITLE:	Platinum complexes and uses therewith			
INVENTOR(S):	Nishi, Seiichi, Kawasaki, Japan Ohishi, Kazuo, Kawasaki, Japan Izawa, Kunisuke, Kawasaki, Japan Shiio, Tsuyoshi, Kamakura, Japan Suami, Tetsuo, Musashino, Japan			
PATENT ASSIGNEE(S):	Ajinomoto Co., Inc., Tokyo, Japan (non-U.S. corporation)			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5041579		19910820	<--
APPLICATION INFO.:	US 1988-257899		19880923 (7)	<--
	NUMBER		DATE	
PRIORITY INFORMATION:	JP 1987-241720		19870926	<--
	JP 1988-211695		19880826	<--
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Shaver, Paul F.			
LEGAL REPRESENTATIVE:	Oblon, Spivak, McClelland, Maier & Neustadt			
NUMBER OF CLAIMS:	6			

EXEMPLARY CLAIM: 1
LINE COUNT: 505
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Platinum complexes of cis-diaminocyclohexanol or cis-diaminocyclohexane, with the exclusion of platinum complexes of 2-deoxystreptamine, having high anti-tumor activity, low toxicity, water-solubility and exhibiting no cross-resistance to cis-platin.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM The starting material cis-dichlorodiaminocyclohexanolplatinum(II) can be easily obtained by adding an aqueous solution of a diaminocyclohexanol hydrochloride or hydrobromide to an aqueous solution of potassium chloroplatinate, neutralizing the reaction mixture with sodium bicarbonate, allowing the resulting solution. . .
DETD 5g (±)-(1/2,3)-2,3-diaminocyclohexanol dihydrochloride was suspended in 3 ml dichloromethane, and thereto 7.48 g triethylamine, 19.8 g Naproxen and 0.3 g dimethylaminopyridine were added. . . filtrated and the precipitate on the filter was washed with methanol:ether (1:1) and ether, and then dried under vacuum. (-)-(1/2,3)-2,3-Diaminocyclohexanol dihydrochloride 1.704 g (yield: 72%) was obtained as a white solid. By the same method as above, from 7.96 g of polar-isomer, (+)-(1/2,3)-2,3-diaminocyclohexanol dihydrochloride 1.6 g (yield: 76%) was obtained as a white solid. (-)-(1/2,3)-2,3-diaminocyclohexanol dihydrochloride:
DETD (+)-(1/2,3)-2,3-diaminocyclohexanol dihydrochloride:
DETD 1.88 g (-)-(1/2,3)-2,3-Diaminocyclohexanol dihydrochloride and 3.84 g K.sub.2 PtCl.sub.4 were dissolved in 28.2 ml water, 1.56 g NaHCO.sub.3 was added thereto, and after stirring. . .
DETD By the same method as above, 0.62 g of (-)-cis-dichloro-(1/2,3)-2,3-diaminocyclohexanolplatinum(II) (yield: 85%) was obtained from 1.83 g (+)-(1/2.3)-2,3-diaminocyclohexanol dihydrochloride and from 2.5 g of this Pt complex, the product of Compound No. 9 (2.60 g) (yield: 90%) was obtained.
IT 121-44-8, Triethylamine, reactions 151-51-9, Carbodiimide 3385-21-5, 1,3-Diaminocyclohexane 10025-99-7 22204-53-1, Naproxen 57951-36-7, Dimethylaminopyridine 116004-49-0 123620-43-9
(reaction of, in preparation of platinum complex antitumor agents)
IT 3385-21-5, 1,3-Diaminocyclohexane
(reaction of, in preparation of platinum complex antitumor agents)
RN 3385-21-5 USPATFULL
CN 1,3-Cyclohexanediamine (CA INDEX NAME)



L79 ANSWER 37 OF 38 USPATFULL on STN
ACCESSION NUMBER: 75:71676 USPATFULL Full-text
TITLE: S-substituted hydropyrimidine compounds
INVENTOR(S): Rickter, Donald O., Arlington, MA, United States
PATENT ASSIGNEE(S): Polaroid Corporation, Cambridge, MA, United States (U.S. corporation)

NUMBER KIND DATE

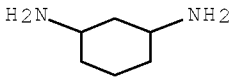
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 3929786		19751230	<--
APPLICATION INFO.:	US 1973-402130		19731001 (5)	<--

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1972-214665, filed on 3 Jan 1972, now patented, Pat. No. US 3785813
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Daus, Donald G.
ASSISTANT EXAMINER: Rivers, Diana G.
LEGAL REPRESENTATIVE: Kiely, Philip G., Matthews, Mart C.
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
LINE COUNT: 465
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel polycyclic S-substituted hydropyrimidine compounds are provided having the general formula: ##SPC1##

Wherein Z.sub.1 represents one or more 5 to 6 member alicyclic or heterocyclic fused rings; R is hydrogen or a carbon atom which is included in Z.sub.1 ; and X is hydrogen or a group replaceable by hydrogen in an hydrolysis reaction with an aqueous alkaline solution. These compounds are useful as development restrainers, particularly in dye developer diffusion transfer photographic processes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD The resultant product, 2-(3',5'-dichloro-4'-hydroxybenzylmercapto)-trans-4,5-cyclopenta-3,4,5,6-tetrahydropyrimidine hydrochloride, illustrates the "salt" form of the development restrainer precursors of the present invention which may occur when the X moiety. . .
IT 3385-21-5
(cyclization of, with carbon disulfide, cyclohexapyrimidinethione from)
IT 3385-21-5
(cyclization of, with carbon disulfide, cyclohexapyrimidinethione from)
RN 3385-21-5 USPATFULL
CN 1,3-Cyclohexanediamine (CA INDEX NAME)



L79 ANSWER 38 OF 38 USPATFULL on STN
ACCESSION NUMBER: 74:3390 USPATFULL Full-text
TITLE: POLYCYCLIC HYDROPYRIMIDINE DEVELOPMENT RESTRAINERS
INVENTOR(S): Rickter, Donald O., Arlington, MA, United States
PATENT ASSIGNEE(S): Polaroid Corporation, Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 3785813		19740115	<--
APPLICATION INFO.:	US 1972-214665		19720103 (5)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted

PRIMARY EXAMINER: Torchin, Norman G.
ASSISTANT EXAMINER: Schilling, Richard L.
LEGAL REPRESENTATIVE: Robert M. Ford et al.
NUMBER OF CLAIMS: 28
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 1138
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A development restrainer is made available during dye diffusion transfer processing after a predetermined period by incorporating in the photographic film unit, an S-substituted, polycyclic pyrimidine compound of the formula ##SPC1##

Wherein Y is a hydropyrimidine group, X is hydrogen in its active or unblocked form or a group hydrolyzable by alkaline processing composition as a function of temperature to provide a controlled release of development restrainer during the development process and Z is a ring system attached to the hydropyrimidine group. Those compounds in which Z is an alicyclic group or a heterocyclic group are novel compositions of matter.

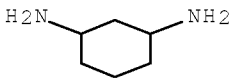
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . a melting point of 229°-233° and was confirmed by elemental analysis to be 2-(3',5'-dichloro-4'-hydroxy-benzylmercapto) - trans 4,5 - cyclopenta-3,4,5,6, -tetrahydropyrimidine hydrochloride, i.e., compound C in the equation above.

IT 51-45-6, reactions 3385-21-5 21544-02-5
(reaction of, with carbon disulfide)

IT 3385-21-5
(reaction of, with carbon disulfide)

RN 3385-21-5 USPATFULL
CN 1,3-Cyclohexanediamine (CA INDEX NAME)



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=> d his full

     (FILE 'HOME' ENTERED AT 08:38:47 ON 20 FEB 2008)

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                E US2006-596994/APPS
L1            1 SEA ABB=ON  PLU=ON  US2006-596994/AP
                SEL RN

     FILE 'REGISTRY' ENTERED AT 08:41:08 ON 20 FEB 2008
L2          196 SEA ABB=ON  PLU=ON  (100-46-9/BI OR 1000417-94-6/BI OR
                1000490-56-1/BI OR 10102-94-0/BI OR 106792-38-5/BI OR 1192-58-1
                /BI OR 1215-59-4/BI OR 131237-81-5/BI OR 132706-12-8/BI OR
                13523-92-7/BI OR 13669-42-6/BI OR 141-82-2/BI OR 141-97-9/BI
                OR 143679-80-5/BI OR 147-71-7/BI OR 154737-90-3/BI OR 156496-64
                -9/BI OR 1578-96-7/BI OR 15861-36-6/BI OR 171919-36-1/BI OR
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                I OR 5652-13-1/BI OR 58630-07-2/BI OR 6041-50-5/BI OR 6188-43-8
                /BI OR 6340-55-2/BI OR 636-61-3/BI OR 645400-43-7/BI OR
                645400-44-8/BI OR 645400-49-3/BI OR 645400-50-6/BI OR 67509-84-
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                83783-33-9/BI OR 860296-28-2/BI OR 860296-29-3/BI OR 860296-30-
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                860296-34-0/BI OR 860296-35-1/BI OR 860296-37-3/BI OR 860296-39
                -5/BI OR 860296-41-9/BI OR 860296-42-0/BI OR 860
L3            8 SEA ABB=ON  PLU=ON  L2 AND 6/C
                D SCA
L4            1 SEA ABB=ON  PLU=ON  "1,3-CYCLOHEXANEDIAMINE"/CN
                SEL RN
L5           80 SEA ABB=ON  PLU=ON  3385-21-5/CRN
                D RN L4
L6              STR 3385-21-5
                D L6
L7            4 SEA FAM SAM L6
                D SCA
                D STAT QUE L7
L8          103 SEA FAM FUL L6
L9            2 SEA ABB=ON  PLU=ON  L2 AND L8
                D SCA
                SAVE TEMP CHA994C11FAM/A L8
L10          23 SEA ABB=ON  PLU=ON  L8 AND CL/ELS
                D SCA
L11           4 SEA ABB=ON  PLU=ON  L10 AND ?HYDROCHLORID?/CNS
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     FILE 'ZCAPLUS' ENTERED AT 08:49:19 ON 20 FEB 2008
L12           5 SEA ABB=ON  PLU=ON  L11

     FILE 'CAOLD' ENTERED AT 08:49:34 ON 20 FEB 2008
L13           0 SEA ABB=ON  PLU=ON  L11

     FILE 'ZCAPLUS' ENTERED AT 08:49:47 ON 20 FEB 2008
L14      422537 SEA ABB=ON  PLU=ON  ?ISOMER?/BI
L15      135031 SEA ABB=ON  PLU=ON  ?CHIRAL?/BI
L16      288070 SEA ABB=ON  PLU=ON  ?STEREO?/BI
L17       93962 SEA ABB=ON  PLU=ON  ?ENANTIO?/BI
L18      382970 SEA ABB=ON  PLU=ON  ?RESOLUTION?/BI
L19      210367 SEA ABB=ON  PLU=ON  ASYMMETR?/BI
L20           3 SEA ABB=ON  PLU=ON  L12 AND L14
L21           0 SEA ABB=ON  PLU=ON  L12 AND L15
L22           1 SEA ABB=ON  PLU=ON  L12 AND L16
L23           0 SEA ABB=ON  PLU=ON  L12 AND L17
L24           1 SEA ABB=ON  PLU=ON  L12 AND L18
L25           0 SEA ABB=ON  PLU=ON  L12 AND L19
L26           3 SEA ABB=ON  PLU=ON  (L20 OR L21 OR L22 OR L23 OR L24 OR L25)
                D SCA
L27     1549726 SEA ABB=ON  PLU=ON  ?SEPARAT?/BI
L28           2 SEA ABB=ON  PLU=ON  L12 AND L27
L29           5 SEA ABB=ON  PLU=ON  L12 OR (L20 OR L21 OR L22 OR L23 OR L24 OR
                L25 OR L26)

     FILE 'REGISTRY' ENTERED AT 08:59:58 ON 20 FEB 2008
L30           9 SEA ABB=ON  PLU=ON  L8 AND 1/NC
                D SCA

     FILE 'ZCAPLUS' ENTERED AT 09:00:55 ON 20 FEB 2008
L31         164 SEA ABB=ON  PLU=ON  L30
L32      192120 SEA ABB=ON  PLU=ON  ?HYDROCHLORID?/BI
L33          21 SEA ABB=ON  PLU=ON  L31 AND L32
L34       92238 SEA ABB=ON  PLU=ON  ?HYDROCHLORID?/AB,ST,TI
L35           4 SEA ABB=ON  PLU=ON  L31 AND L34
                D SCA
L36          17 SEA ABB=ON  PLU=ON  L33 NOT L35
                D SCA
L37          17 SEA ABB=ON  PLU=ON  CYCLOHEXANEDIAMINE DIHYDROCHLORID?/BI
                D SCA
L38           1 SEA ABB=ON  PLU=ON  L33 AND L37
L39        9895 SEA ABB=ON  PLU=ON  HYDROCHLORIDES/BI
L40           1 SEA ABB=ON  PLU=ON  L39 AND L33

     FILE 'REGISTRY' ENTERED AT 09:13:27 ON 20 FEB 2008
L41        9478 SEA ABB=ON  PLU=ON  ?CYCLOHEXANEDIAMINE?/CNS
L42          33 SEA ABB=ON  PLU=ON  L41 AND IDS/CI
                D SCA
L43           1 SEA ABB=ON  PLU=ON  CYCLOHEXANEDIAMINE/CN
                D SCA

     FILE 'ZCAPLUS' ENTERED AT 09:16:18 ON 20 FEB 2008
L44         137 SEA ABB=ON  PLU=ON  L43
L45           1 SEA ABB=ON  PLU=ON  L34 AND L44
                D SCA
L46          32 SEA ABB=ON  PLU=ON  1,3/BI AND L44
L47           3 SEA ABB=ON  PLU=ON  L32 AND L44
                D SCA
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L48           1 SEA ABB=ON  PLU=ON  L45 AND L47
L49           7 SEA ABB=ON  PLU=ON  L44 AND L14
                D SCA

     FILE 'USPATFULL' ENTERED AT 09:21:39 ON 20 FEB 2008
L50           1 SEA ABB=ON  PLU=ON  L11
L51      155006 SEA ABB=ON  PLU=ON  ?HYDROCHLORID?
L52           1 SEA ABB=ON  PLU=ON  L50 AND L51
                D SCA
                D KWIC
L53          72 SEA ABB=ON  PLU=ON  L30
L54          27 SEA ABB=ON  PLU=ON  L51 AND L53
L55          14 SEA ABB=ON  PLU=ON  L54 AND PD<20040107
L56          16 SEA ABB=ON  PLU=ON  L54 AND PRD<20040107
L57          21 SEA ABB=ON  PLU=ON  L54 AND AD<20040107
L58          23 SEA ABB=ON  PLU=ON  (L55 OR L56 OR L57)
                D KWIC 1-5
L59          18 SEA ABB=ON  PLU=ON  CYCLOHEXANEDIAMINE (10A) ?HYDROCHLORID?
                D KWIC 1-3
L60           1 SEA ABB=ON  PLU=ON  L58 AND L59
L61           1 SEA ABB=ON  PLU=ON  1,3 (3W) L59
                D KWIC
L62         214 SEA ABB=ON  PLU=ON  1,3 (3W) CYCLOHEXANEDIAMINE
L63          29 SEA ABB=ON  PLU=ON  L62 AND L51

     FILE 'STNGUIDE' ENTERED AT 09:30:42 ON 20 FEB 2008
                D COST

     FILE 'REGISTRY' ENTERED AT 09:32:51 ON 20 FEB 2008
L64           0 SEA ABB=ON  PLU=ON  L2 AND ?CARBAMATE?/CNS
L65          39 SEA ABB=ON  PLU=ON  L2 AND 3/NRS
                D SCA
                E "CARBAMIC ACID, N,N'-(1R,3R)-1,3-CYCLOHEXANEDIYLBIS-, C,C'-BI
L66           1 SEA ABB=ON  PLU=ON  "CARBAMIC ACID, N,N'-(1R,3R)-1,3-CYCLOHEXAN
                EDIYLBIS-, C,C'-BIS(PHENYLMETHYL) ESTER, REL-"/CN
                D SCA
                D RSD
L67           5 SEA ABB=ON  PLU=ON  L2 AND (46.150.1/RID AND (>1 46.150.18/RID)
                 AND N>1 AND O>1)
                D SCA
L68           3 SEA ABB=ON  PLU=ON  L67 AND 3/NRS
                D SCA
                D RN 1
L69             STR 860434-15-7
                D
L70           0 SEA FAM SAM L69
L71           3 SEA FAM FUL L69
                D SCA

     FILE 'ZCAPLUS' ENTERED AT 09:44:10 ON 20 FEB 2008
L72           3 SEA ABB=ON  PLU=ON  L71

     FILE 'BEILSTEIN' ENTERED AT 09:45:12 ON 20 FEB 2008
L73           0 SEA FAM SAM L69
L74           2 SEA FAM FUL L69

     FILE 'WPIX' ENTERED AT 09:46:07 ON 20 FEB 2008
L75           0 SEA FAM SAM L69
L76           0 SEA FAM FUL L69
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     FILE 'STNGUIDE' ENTERED AT 09:48:19 ON 20 FEB 2008

     FILE 'REGISTRY' ENTERED AT 09:48:41 ON 20 FEB 2008

     FILE 'ZCAPLUS' ENTERED AT 09:48:47 ON 20 FEB 2008
                D STAT QUE L29
                D STAT QUE L35
                D STAT QUE L38
                D STAT QUE L40
                D STAT QUE L45
                D STAT QUE L48
                D STAT QUE L72
L77           12 SEA ABB=ON  PLU=ON  L29 OR L35 OR L38 OR L40 OR L45 OR L48 OR
                L72

     FILE 'BEILSTEIN' ENTERED AT 09:49:43 ON 20 FEB 2008
                D STAT QUE L74

     FILE 'WPIX' ENTERED AT 09:49:59 ON 20 FEB 2008
                D STAT QUE L76

     FILE 'USPATFULL' ENTERED AT 09:50:09 ON 20 FEB 2008
                D STAT QUE L50
                D STAT QUE L53
                D STAT QUE L52
                D STAT QUE L60
                D STAT QUE L58
                D STAT QUE L61
L78           24 SEA ABB=ON  PLU=ON  L50 OR L52 OR L60 OR L58 OR L61

     FILE 'STNGUIDE' ENTERED AT 09:51:14 ON 20 FEB 2008

     FILE 'ZCAPLUS, BEILSTEIN, USPATFULL' ENTERED AT 09:51:27 ON 20 FEB 2008
L79           38 DUP REM L77 L74 L76 L78 (0 DUPLICATES REMOVED)
                       ANSWERS '1-12' FROM FILE ZCAPLUS
                       ANSWERS '13-14' FROM FILE BEILSTEIN
                       ANSWERS '15-38' FROM FILE USPATFULL
                D IBIB ABS HITIND HITSTR L79 1-12
                D IDE ALLREF L79 13-14
                D IBIB ABS KWIC HITSTR L79 15-38


     FILE HOME

     FILE ZCAPLUS

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     FILE LAST UPDATED: 19 Feb 2008  (20080219/ED)

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 19 FEB 2008 HIGHEST RN 1004621-14-0
DICTIONARY FILE UPDATES: 19 FEB 2008 HIGHEST RN 1004621-14-0

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FILE CAOLD
FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 19 Feb 2008 (20080219/PD)
FILE LAST UPDATED: 19 Feb 2008 (20080219/ED)
HIGHEST GRANTED PATENT NUMBER: US7334268
HIGHEST APPLICATION PUBLICATION NUMBER: US2008040827
CA INDEXING IS CURRENT THROUGH 19 Feb 2008 (20080219/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 19 Feb 2008 (20080219/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2007
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2007

FILE STNGUIDE
FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Feb 15, 2008 (20080215/UP).

FILE BEILSTEIN
FILE LAST UPDATED ON January 3, 2008

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FILE COVERS 1771 TO 2007.
 FILE CONTAINS 10,119,480  SUBSTANCES

>>>PLEASE NOTE: Reaction Data and substance data are stored in
   separate documents and can not be searched together in one query.
   Reaction data for BEILSTEIN compounds may be displayed
   immediately with the display codes PRE (preparations) and REA
   (reactions).  A substance answer set retrieved after the search
   for a chemical name, a compounds with available reaction
   information by combining with PRE/FA, REA/FA or more generally
   with RX/FA. The BEILSTEIN Registry Number (BRN) is the link
   between a BEILSTEIN compound and belonging reactions. For mo
   detailed reaction searches BRNs can be searched as reaction
   partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

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FILE WPIX
FILE LAST UPDATED:                      13 FEB 2008   <20080213/UP>
MOST RECENT THOMSON SCIENTIFIC UPDATE:     200811     <200811/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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